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FORMERLY The BULLETIN

APPLICATION OF CHELATING AGENTS IN PHARMACY AND MEDICINE

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Dear Sirs:

Interested in Internship

DEAR SIRS: Your address has been recommended by the American Council on Pharmaceutical Education. I am a Tehran University graduate in Pharmacy (Pharm. D.), and I would like to receive an assistantship or obtain an internship in a hospital pharmacy in the United States to do further work in pharmacy, so I respectfully ask your advice as to the possibility of obtaining a hospital pharmacy internship for the winter or spring term of 1960.

I have studied the announcement of the University of California, School of Pharmacy 1958-1959. The curriculum in Tehran School of Pharmacy, which is an accredited school and leads to the degree Doctor of Pharmacy, is nearly the same as the curriculum in the School of Pharmacy, University of California. If it is necessary, I would be glad to send my official transcripts by the next mail.

Any information you can give relative to finding possibilities for an internship will be greatly appreciated.

If it appears that it will not be possible to obtain a hospital pharmacy internship for the winter or spring term of 1960, the writer would be grateful for any advice or suggestions you may have.

Thank you very much for your kind consideration of this inquiry.

DR. AMINOLLAH MANSOUR

Ave. Bahar, Karkhaneh
Conservesazi Sazeman
Barnameh
Mashad, Iran

Journal to be Used in Course

DEAR SIRS: We are giving some thought to using the AMERICAN JOURNAL OF HOSPITAL PHARMACY in our course in hospital pharmacy at the University of Tennessee. This will be a required course involving sixty seniors.

Could this be handled best by bulk mailing or individual subscriptions? Also, is there a special student rate or are individual subscriptions $4.50 per year?

Thanks for your help.

GROVER C. BOWLES, JR., *Director*

Department of Pharmacy
Baptist Memorial Hospital
Memphis, Tennessee

EDITOR'S NOTE: At the present time, the JOURNAL is available on subscription at $4.50 per year and there is no special rate for students.

We have found it advantageous to handle these as single subscriptions rather than bulk mailings. Subscriptions to the JOURNAL must begin either in July or in January. In this instance, it would be advisable to suggest that the subscriptions begin in July and the back issues (July and August) can be sent to the students immediately on receipt of order. It would facilitate handling the total order if the list of subscribers could be sent at one time to the Division of Hospital Pharmacy, 2215 Constitution Avenue, N.W., Washington, D. C.

Reprints Requested

DEAR SIRS: I have read a review dealing with "Identification Guide for Solid Dosage Forms," in the AMERICAN JOURNAL OF HOSPITAL PHARMACY 15:313 (1958). I should be obliged if you could send me a reprint.

J. MAHY

Department of Galenical Pharmacy
University of Brno
Brno, Czechoslovakia

Comments on Formulary Service

DEAR SIRS: *The American Hospital Formulary Service* has been distributed to the Nursing Divisions and Departments in our hospital and we would like to place an order for six additional copies. . . We would also like to have our hospital's name printed on the cover.

When I was on duty at the A.Ph.A.—ASHP booth at the recent Convention of the Catholic Hospital Association in St. Louis, great interest was shown in the Formulary. Again, congratulations to you and the Committee for a job well done.

GEORGE V. HORNE, *Chief Pharmacist*

The Jewish Hospital
St. Louis, Missouri

DEAR SIRS: Thank you for your letter in which you enclosed a booklet giving information about the *American Hospital Formulary Service* with a listing of the monographs included. This booklet is most helpful and we appreciate it very much.

We are looking forward to receiving the copy of the Formulary as soon as it is off the press.

MAJOR ELSIE VAN PELT, *Administrator*

Booth Memorial Hospital
Cleveland, Ohio

by DON E. FRANCKE

The ASHP and The Hahnemann Case

► THE PRINCIPLE OF PRIOR CONSENT, under which the medical staff authorizes the pharmacist to dispense drugs under their non-proprietary names, has been used in American hospitals for more than a century and has been formalized within the past quarter-century. Only recently has this principle been challenged by a Board of Pharmacy. This challenge took the form of an Adjudication and Order by the Pennsylvania Board of Pharmacy suspending the license of the Chief Pharmacist of Hahnemann Hospital, Philadelphia, for alleged substitution. Hahnemann Hospital operates under the formulary system and the medical staff has authorized the Chief Pharmacist to dispense drugs under their non-proprietary or official names. This challenge has been met by Hahnemann Hospital, and of necessity its medical staff will be involved, through the filing of an appeal on behalf of the Chief Pharmacist and the filing of a series of 42 exceptions to the adjudication of the State Board of Pharmacy with the Court of Common Pleas of Dauphin County.

This case raises serious questions of policy for the SOCIETY. The ASHP position on the "Formulary System and Alleged Substitution" has been clearly stated. (*Bull. Am. Hosp. Pharm. 14*:691 Nov.-Dec. 1957.) This position approves the dispensing of drugs under their non-proprietary names, but only when the medical staff has given its prior approval in writing. What, then, should the SOCIETY do when a Board of Pharmacy takes action to suspend one of its members operating under a formulary system where such prior consent exists? Obviously, the ASHP cannot enter every legal case in which hospital pharmacists in one or more of the 50 states become involved. At the same time, it cannot in good judgement ignore challenges to basic principles which are important to hospitals, their medical staffs, patients, and hospital pharmacists.

In order to resolve this conflict and to arrive at a general policy, President Bogash called a meeting in Philadelphia on July 14 of representatives of various organizations interested in this problem. After full discussion it was agreed that the SOCIETY should express its sympathetic interest in the Hahnemann case but should refrain from entering the case on a national level at this time. At the same time, however, it was decided that the SOCIETY should engage counsel to advise it on matters of legal significance with respect to the formulary system. This policy is, in general, similar to that followed by, for example, the American Hospital Association and other national organizations when matters involving areas of the organization's interests arise on a local basis.

Under this policy the ASHP will be able to obtain advice on matters of legal principle without becoming involved in a number of local legal skirmishes. Thus, the ASHP will be able to conserve its strength and at the same time receive counsel which will be helpful not only to the national organization itself but also, when transmitted, to its affiliated chapters and individual members.

Following this decision, Mr. S. Walter Foulkrod was engaged on a retainer basis to advise the SOCIETY. Mr. Foulkrod is a well-known Philadelphia attorney, a professor of pharmaceutical law at Temple University, and one who has had extensive experience in drafting and interpreting pharmaceutical legislation.

With this policy adopted, the SOCIETY is in a flexible position to sustain the principle of prior consent and to take other actions which may be indicated by future events.

by ROBERT W. MAHONEY

► CHELATING AGENTS AND CHELATE COMPOUNDS HAVE become increasingly useful entities in pharmacy and medicine during recent years. It is the purpose of this paper to examine in general their composition and mechanisms of action, and then to delve more thoroughly into specific pharmaceutical and medical applications.

Chemistry

Chelating compounds are exemplified by an organic molecule exhibiting two or more coordinate bonding groups in the proper spatial arrangement; thus allowing the simultaneous bonding of a multivalent metallic ion. The resulting chelate is a heterocyclic ringed complex incorporating the metal ion as an integral part of the ring. As a consequence of such firm bonding the complex is virtually un-ionized, and there is a profound change in the physical, chemical, and biological properties of the participating ion. For example, the calcium chelate of ethylenediamine tetraacetic acid will not give any of the characteristic tests for the calcium ion—no precipitate with phosphate, carbonate, hydroxide, or even oxalate. The situation produced is similar to the physical removal of the ion; nevertheless, the metal is still present—only in a chelated form.

The name chelate, originated by Morgan and Drew in 1920, is taken from the Greek *chele* meaning a crab's claw. Consideration of the structural repre-

ROBERT W. MAHONEY M.Sc. recently completed the internship program in hospital pharmacy at the University of Michigan in Ann Arbor.

APPLICATION OF

sentation of the compounds in Figure 1 shows this term to be an apt one.

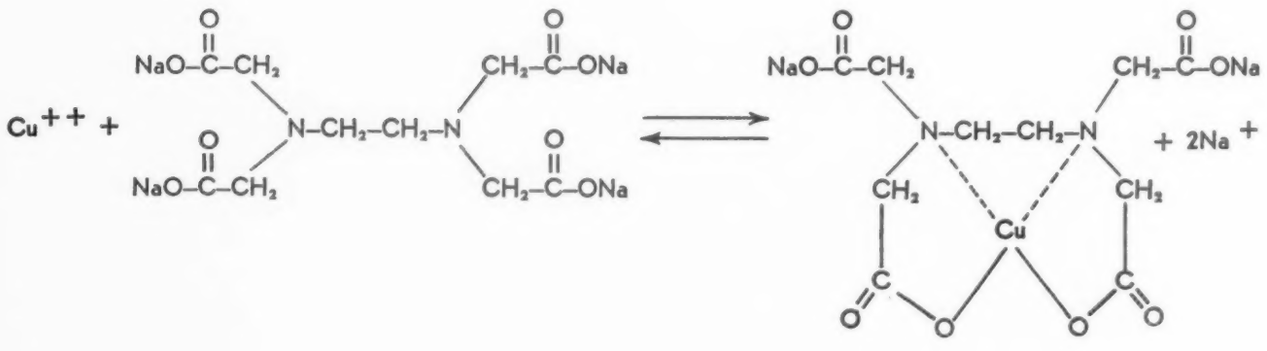
Although the electron donor centers (chelation sites) within the chelating agents are limited almost entirely to nitrogen, oxygen, and sulfur, the cation within the chelate may represent a wide variety of metals. These metals exhibit a definite order of chelation, although this can be shown to be a function of the *p*H of the reaction medium. Since the strength of the metal-chelate bond is a reflection of its stability, we may formulate an equation representing this property. The stability constant may be written as $K = \frac{(MA^{m-n})}{(M^{+m})\ (A^{-n})}$, where M^{+m} represents the metal ion and A^{-n} the chelating agent. A metal having a higher value for K, *i.e.*, one which is more stable, will displace those of a lower order. Table I lists the stability constants for certain metal chelates of ethylenediamine tetraacetic acid (EDTA), one of the most powerful chelating agents yet discovered.

Table I. Stability of Various Metal Complexes with EDTA

Metal Ion	Log K
Ni	18.4
Cu	18.3
Pb	18.2
Zn	16.1
Co	16.1
Mn	13.4
Ca	10.6
Mg	8.7
Na	1.7

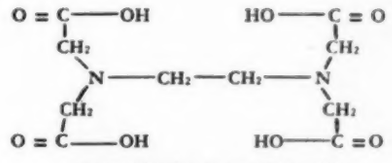
It might be well to mention that *in vitro* chelating ability may not truly depict activity under physiological conditions, for such factors as steric hinderance, competition with the body's natural complexing agents, and endogenous metals may influence the mechanism.

Although there exists a rather impressive number of potent chelating compounds, the majority of them have not been studied for pharmaceutical and pharmacological action.[51] However, perhaps the mechan-

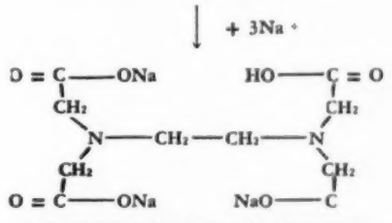


isms and possible uses of these substances are best typified by EDTA and, because there is an abundance of information on this preparation, special attention will be directed toward it.

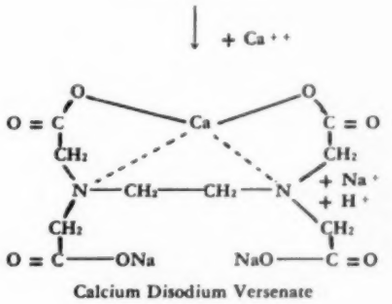
EDTA is a synthetic polyaminocarboxylic acid also known as ethylene *bis*-iminodiacetic acid and ethylene dinitrilotetraacetic acid. Since it is a tetrabasic acid, EDTA will form a series of mono, di, tri, and tetra sodium salts, increasing in water solubility with increasing degree of neutralization. The salts of EDTA are nonhygroscopic and are stable on prolonged heating. Moreover, their aqueous solutions do not support mold growth nor do they hydrolyze or deteriorate. The fact that the metal chelates of EDTA and its salts are water soluble and virtually undisassociated, forms the basis for their application to pharmaceutical and medical problems.



ethylenediamine tetra-acetic acid



ethylenediamine hydrogen trisodium acetate
(Sodium Versenate)



Calcium Disodium Versenate

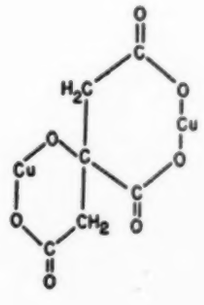
Applications in Pharmacy

For many years chelating agents have played an important role in the preparation of pharmaceutical products, although perhaps not recognized as such. The use of the citrate and tartrate ion in many galenicals, *e.g.* ferric ammonium citrate; iron, quinine, and strychnine elixir; soluble ferric phosphate; anticoagulant sodium citrate, is based upon their ability to chelate insoluble metal ions to form a water soluble chelate (sequestration). In addition, many nonofficial remedies make use of the sequestering ability of these ions to solubilize such metals as magnesium, manganese, iron, calcium, and copper.

Although industry has for many years employed synthetic chelating agents in the manufacture of rubber, paints, plastics, foods, and cosmetics, it has only been within the last decade that these agents have influenced the formulation of pharmaceuticals. In general, the purpose of these compounds is to chelate and thereby deactivate the traces of heavy metals which cause precipitation from solutions, development of color, oxidation, and other forms of deterioration.

Stabilization of Drugs

The stability of emulsions may be enhanced and solution clarity improved by the addition of small amounts of EDTA (0.1 to 1%); likewise, the production of "off" colors and odors in liquid medications is prevented by the same chelating mechanism. Solutions of antibiotics and vitamins are particularly susceptible to decomposition when trace amounts of heavy metals are present to exert a catalytic effect. EDTA can, by virtue of its chelating action, inactivate these ions and thereby extend product life. Chain *et al* have reported that alcoholic solutions of penicillin salts may be stabilized by incorporating a synthetic chelator into the formulation.[13] Similar results were observed by Swallow, who noted that addition of small



amounts (1:500) of tetrasodium EDTA to aqueous penicillin solutions markedly reduced their loss of potency.[72] Oxytetracycline has also been reported to have been stabilized by the same means. The copper catalyzed degradation of ascorbic acid solutions is delayed by inclusion of tetrasodium EDTA; however, a liquid formulation of ascorbic acid and cyanocobalamin is only partially protected under similar conditions.[5,44] This negation of metal induced deterioration is not limited to antibiotic or vitamin solutions by any means. Various papers relate the efficacy of these compounds in stabilizing solutions of procaine, para-aminosalicylates, and epinephrine when Na_2 EDTA is used in concentrations of 0.5 to 1.5 percent. An important fact is that in all cases therapeutic effectiveness was not impaired in any manner.

The observation that higher blood levels of chlortetracycline resulted from oral dosage when EDTA was simultaneously administered,[21] has prompted the study of more stable and longer acting metal-antibiotic chelates.[30]

Analytical

EDTA enjoys an enviable position as a versatile reagent in analytical chemistry. In citing the contributions to pharmaceutical assay, it would suffice to mention that the U.S.P. method for determining the calcium content of official preparations involves a period of three to three and a half hours, whereas a proposed EDTA procedure could be completed within 15 minutes with the same degree of accuracy.[35,52]

The effectiveness, advantages, and the multiplicity of application of chelating agents are becoming increasingly recognized, and their future use in pharmacy is limited only by the profession's knowledge of their fascinating properties.

Applications in Medicine

Chenoweth states that a chelating agent can physiologically influence the cellular constituents of the body via the following mechanisms: (1) acquisition of unwanted metal ions, (2) removal of metals from intact organism, and (3) reaction with fixed intracellular metals.[14] In original clinical applications chelating agents were employed to remove the unwanted metal from an organism; the metal was bound into an innocuous chelate which was rapidly excreted in the urine.

Calcium Levels

In a series of animal experiments Popovici *et al.* demonstrated that the disodium salt of EDTA caused a distinct lowering of the serum calcium level, although the degree of hypocalcemia was a function of the mode of administration, concentration of solution, and rapidity of injection.[58] Later, Spencer noted that a slow intravenous infusion of the drug produced excess calcinuria without a significant change in the serum calcium level. This is indicative of the prompt spontaneous replenishment of ionized calcium from the skeletal deposits.[70]

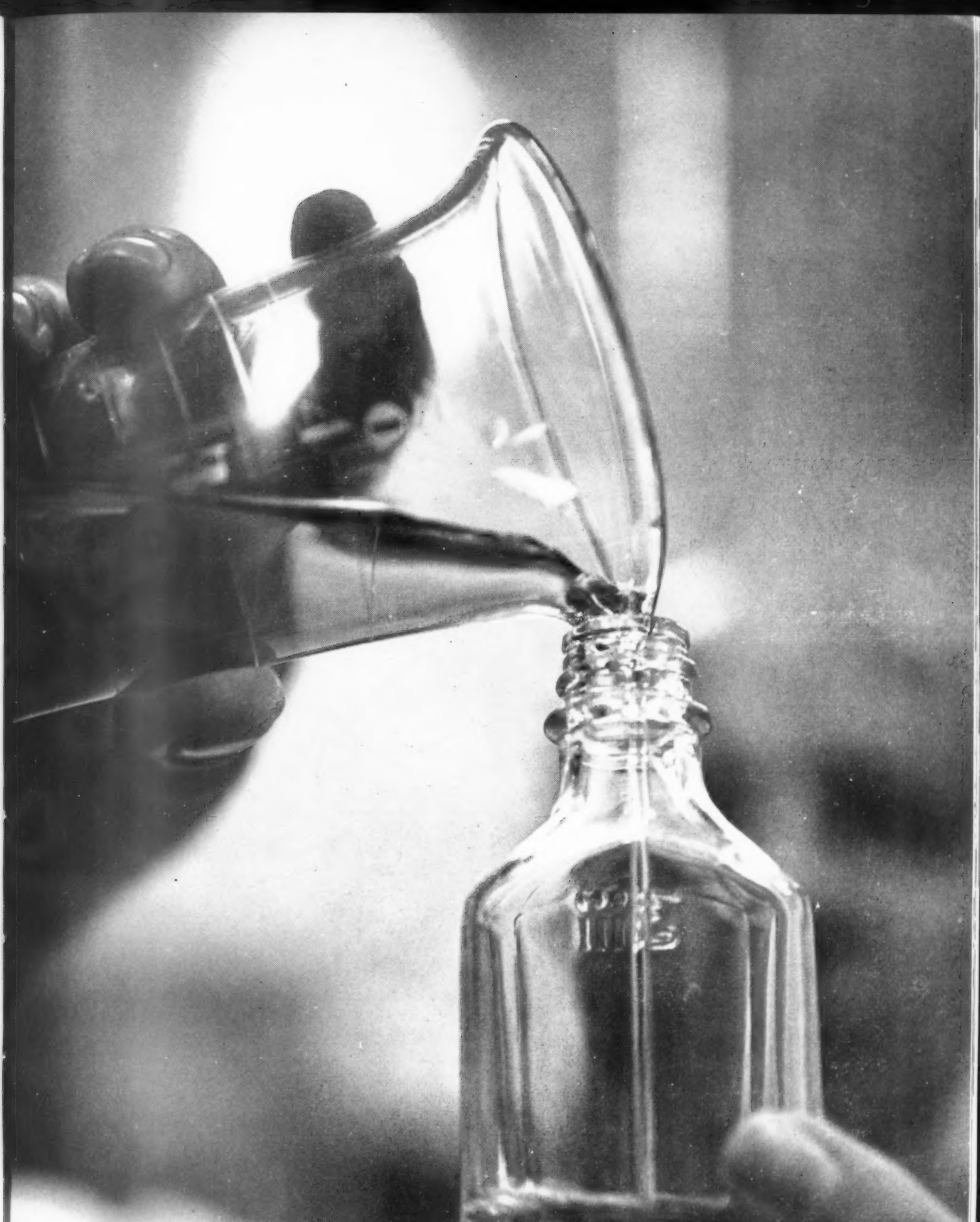
In the hope that this compound would prove useful in lowering extremely high levels of serum calcium, it was tried in a number of cases of metabolic calcium disorders, osteolytic metastasis, and hypervitaminosis D. The results varied; however, Dudley ascribes to the drug certain renal damage such as tubular hemorrhage, engorgement of the reticulo-endothelial cells, and severe damage to the renal tubule.[20] Even though the onset of serum calcium depression is rapid, Holland *et al.* relate that it is of short duration and no clinical benefit.[42]

For chelating action within the body, other than treatment of elevated calcium serum levels, the calcium disodium EDTA chelate (Edathamil N.N.D.) is employed so that a negative calcium balance does not occur. Foreman *et al.* have shown that calcium EDTA labeled with C^{14} passes through the body unchanged, with 95 to 98 percent of the parenterally administered dose being excreted in the urine within six hours.[29] Oral administration results in poor absorption as does cutaneous application.[27] Others, however, note that the application of a 5 percent EDTA washable ointment caused a definite decrease in serum calcium.[58]

Lead Intoxication

In the past, low calcium diets, high phosphorus diets plus magnesium sulfate, and the administration of citrates have been used to mobilize lead in cases of lead intoxication. BAL (dimercaprol) was suggested as a method of treatment because of its success in counteracting the toxic effects of arsenic and mercury. Unfortunately it appears as though the lead-BAL complex is potentially more toxic than the lead ion itself. Fried *et al.* have interfered with the body's metabolic cycle to produce excess citrate in the hope of stimulating urinary lead excretion.[32]

The rationale for using calcium EDTA in treating lead poisoning is based upon the fact that the lead EDTA chelate has a higher stability constant than the administered calcium chelate. *In vivo* this is verified when ionic plasma lead displaces the calcium from the chelate and is rapidly excreted as the innocuous lead EDTA chelate. The marked stimulation of urinary lead is due to the increased plasma level of ionic lead resulting from EDTA disturbance of the equilibrium between lead in the blood cells and lead in the plasma.[9,73,74]



Bessman, Reid, and Rubin appear to have been the first to employ calcium EDTA therapy in cases of lead encephalopathy.[10] Since that time well documented studies have shown this agent to be the drug of choice.[6,7,11,18,26,40,48,49,60] The recommended course of therapy is one to two grams of the drug per day for an adult, given by intravenous infusion. Higher total lead excretion will result if therapy is interrupted after five days and resumed after a two day rest period. Because of poor absorption, the average oral adult dose is four grams, given in divided doses.

There usually is a 10 to 40 fold increase in urinary lead excretion on the first day of intravenous administration. Oral dosage produces a gradual rise reaching its maximum of a 5 to 10 fold increase by the third or fourth day.[68] One investigator has found that in the management of chronic plumbism, urinary lead is higher when treatment is administered at weekly intervals rather than on a daily basis.

The indiscriminate use of calcium EDTA during long term therapy has been cautioned against by Foreman *et al.*[25] They have observed that hydropic degeneration of the proximal tubules occurs on long time use of this compound, although the lesions are reversible and clear upon cessation of therapy. Perry and Schroeder reported peculiar mucocutaneous lesions resembling avitaminosis B and a six fold increase in renal loss of zinc in a patient given calcium EDTA.[55] Cotter was able to show that while serum metals were slightly affected during calcium EDTA therapy, the plasma copper, sodium, magnesium, and calcium levels were normal one month after treatment.[18]

Other Metals

Detailed case reports have indicated that edathamil is beneficial in treating poisoning by other metals such as vanadium,[53] cadmium,[15] copper,and nickel. Since the LD_{50} of calcium EDTA is 3000 mg./Kg. and the effective doses in heavy metal poisoning are less than 500 mg./Kg., the margin of safety is quite high. The toxicity of the metallic ions is significantly reduced upon chelation: nickel 7000 percent, copper 400 percent, and beryllium 400 percent.[3] In mercurialism, BAL is the drug of choice rather than calcium EDTA. It should be mentioned that BAL was one of the first synthetic chelating agents to be used for heavy metal poisoning. An excellent review of its mode of action and uses has been made by Stocken and Thompson.[71]

Radioactive Metals

With the advent of widespread governmental and industrial use of fission products the problem of heavy metal poisoning has become more profound. Radioactive metals, even in small quantities, are capable of carrying lethal amounts of ionizing radiation into the body. It is imperative that such radioelements be removed as soon as possible to prevent their deposition in the body's skeleton.

DTPA and Plutonium

Previous attempts to eliminate these toxic substances from the body have included low calcium diets, ammonium chloride, calcium gluconate, low phosphorus diets, and zirconium citrate. Only the last agent has shown any degree of success.[24] Experimentally, it was demonstrated that if animals were treated with calcium EDTA within one hour after an injection of Y^{91}, 80 percent of the isotope was excreted as compared with only 29 percent excretion in the controls. If the chelate was injected prior to administration of the radiometal, elimination was 93 percent complete.[17] Hamilton and Scott determined that the metabolic pattern of plutonium was not altered significantly by either oral or intravenous EDTA treatment, once the metal had become fixed within the body.[39] However, later studies demonstrated that it was possible to remove deposited plutonium, although the process was long and tedious.[28] Recently Smith has discovered that a new substance, diethylenetriamine pentaacetic acid (DTPA), was consistantly more effective than EDTA in the removal of deposited plutonium.[69] With prompt treatment, DTPA removed 91 percent of deposited plutonium as compared with 56 percent with EDTA and 39 percent in controls. To date, chelation studies have also been performed on strontium,[16] cerium and lanthanum, and uranium.

An interesting outgrowth of the above studies is the proposal to use a Y^{90} chelate as a means to deliver high ionizing radiation to a selective tissue site, particularly the stomach and bone.[19] This method was was proposed after it was learned that by proper manipulation it is possible to control the site of deposition of this isotope.

Urinary Calculi

One of the earliest applications of EDTA was in the treatment of urinary calculi.[1,47,59] Since these stones are generally composed of insoluble calcium salts such as the oxalate, phosphate, and carbonate, it was thought that an irrigation of EDTA would solubilize the calcium and thus destroy the calculi. *In vitro* studies verified this hypothesis, a 50 percent EDTA solution being even more effective than the standard Suby G Solution. Unfortunately, in clinical practice, a solution of this concentration produced irritation of the bladder epithelium. Much lower concentrations, 1.5 to 3 percent, were still successful in 4 of 7 patients, although again there were reports of minor irritation.[33]

Corneal Calcium Opacities

Along similar lines, Grant successfully employed a 0.01 M disodium EDTA solution to dissolve corneal calcium opacities.[34] While a citrate solution was better tolerated, the EDTA liquid proved to be the most effective agent for these conditions. Later, Breinin and Devoe used the solution in slightly higher concentrations to treat lime burns as well as band keratopathy.[12]

Anticoagulant

Disodium EDTA has also proved satisfactory as an anticoagulant in routine hematological work. Its chief advantages over the oxalate are longer preservation of the cellular elements and lesser effect on cell shrinkage.[38,78] In a comparison of EDTA, heparin, and oxalate, EDTA was found to be far superior in routine packed cell volume, white cell count, and blood smear morphology.[64] Zucker reports the EDTA also has a pronounced effect upon thrombin and prothrombin.[79]

Hypersensitivity to Metals

It is not unusual in clinical practice to find individuals who are allergic to certain metals. The exposure to a particular metal usually causes the development of an eczematous reaction in hypersensitive persons. In a recent publication, Everall and Truter report that both oral dosage and a barrier cream of calcium EDTA afford complete protection against the allergenic effect of nickel in a hypersensitive individual.[22] This work is in harmony with earlier reports of the loss of allergenic property when nickel sulfate solutions were mixed with EDTA.

Skin ulcers produced by repeated exposure to metals are normally difficult to heal; however, Maloof has observed favorable response to EDTA treatment. An ointment of 10 percent EDTA in hydrous wool fat applied to chronic cutaneous chrome ulcers affected complete recovery in each of the 54 reported cases.[50]

Contrast Medium

The apparent lack of toxic effects of the lead EDTA chelate suggested its possible use as a roentgenographic contrast medium. Sapeika administered the compound by oral, intravenous, and subcutaneous routes, and obtained excellent contrast of the gastrointestinal tract, kidney, and bladder.[63] Shapiro agrees that good contrast is obtained on all organs; however he finds the lead EDTA complex too toxic for clinical application.[67] This view seems to be substantiated by recent investigation which uncovered histological renal damage in animals following intravenous injection of the lead chelate.[43] It is mentioned, however, that the renal changes may be due to the action of the EDTA portion *per se*.

Chelation and Antimicrobial Action

The property of chelation is exhibited by many of our antibacterial drugs. Oxime (8-hydroxyquinoline) was one of the first compounds to be examined in an effort to correlate chelating ability with antimicrobial action.[2] While the precise mechanisms of their activity are unknown at present, many of the antituberculous drugs—para aminosalicylate, streptomycin, isoniazid—and antibiotics—chlorotetracycline, oxytetracycline, tetracycline—seem to depend somewhat upon a metal binding property for their action. It is known that other factors are important, since the metabolic products of tetracycline still possess chelating ability, but are devoid of antimicrobial action.[76]

Metal Balance

As previously related, the body possesses numerous natural chelating agents in the form of carbohydrates, proteins, and amino acids. The physiological import of the interplay of these entities with trace metals cannot be overemphasized when one considers the myriad of dependent reactions.

Trace metals themselves have the potentiality of causing or contributing to a disease via several mechanisms. A mutual balance between trace metals is known to exist, which when dearranged may result in definite clinical syndromes; many enzyme systems require a trace metal as an integral constituent; and lastly, trace metals often exert a catalytic effect upon enzyme systems involved with the body's metabolic process.

Recent investigation has supported the theory that chelation therapy could be utilized to counteract the toxic effect of an accumulation of endogenous metals as well as metallic poisoning by environmental exposure. Porphyria is thought to be caused by a cation block, perhaps zinc or copper, of several metalloenzyme systems which are necessary for porphyrin biosynthesis; such a blockade exhausts the body's natural chelators.[56,57] By using synthetic chelators to replenish the body's supply, the clinical picture is improved, although the basic disease is not cured. Peters mentions that BAL and calcium EDTA therapy of porphyria resulted in clinical improvement in 31 of the 37 patients treated.[56]

Wilson's disease (hepatolenticular degeneration) is characterized by a state of positive copper balance, resulting in increased concentrations of copper in the tissue, spinal fluid, and urine. Although parenteral BAL therapy was the treatment of choice in the past, the injections were painful over the long course of medical care. Recently the compound penicillamine, a chelator, was introduced as treatment in this disease and has shown encouraging performance. The com-

pound is as effective as BAL and may be given orally.[75]

The urinary excretion of iron is enhanced 4 to 10 times in hemochromatic patients following intravenous administration of calcium EDTA[23] and Versenol.[66] The only untoward effect observed was diarrhea in one patient receiving a total of 40 grams of the chelate. Isotopic studies indicate that an iron EDTA chelate administered orally was as beneficial in hemoglobin regeneration as equivalent doses of ferrous sulfate, and was less likely to produce adverse effects.[31,65,77]

Clinical Studies

One last application of chelating agents concerning trace metals is their manipulation to allow closer study into the functions of trace metals and their physiological importance. Experimentally, the clinical syndrome of a variety of diseases can be produced through chelation of strategic metals. For example, the signs and symptoms of diabetes mellitus can be brought about by selective chelation of zinc in the pancreatic islet cells.[41,45]

While it is beyond the scope of this paper to examine in detail the experimental and investigation uses of medical chelating agents, it should be mentioned that work is being carried out in the following areas: antidotes for nerve gases,[4] treatment of anticholinesterase intoxication,[36] antagonist of digitalis toxicity,[37,62] counteraction against bacterial toxins,[54] and treatment of scleroderma.[61]

Present-day applications coupled with ever increasing research point to the increased use of chelating agents in pharmacy and medicine in the future.

Selected Bibliography

1. Abeshouse, B.S. and Weinberg, T.: Experimental Study of Solvent Action of Versene on Urinary Calculi, *J. Urol. 65*:316 (1951).
2. Albert, A., Rubbo, S.D., Goldacre, R. J., and Balfour, B. G.: The Influence of Chemical Constitution on Antibacterial Activity, *Brit. J. Exper. Path. 28*:69 (1947).
3. Anon: Use of Calcium Ethylenediamine Tetracetate in Treatment of Heavy Metal Poisoning, Conference. *A. M. A. Arch. Indust. Hyg. 7*:137 (1953).
4. Askew, B. M.: Oximes and Atropine in Sarin Poisoning, *Brit. J. Pharm. 12*:340 (1957).
5. Bartilucci, A. and Foss, N. E.: A Study of the Stability of Cyanocobalamin and Ascorbic Acid in Liquid Formulations, *J. Am. Pharm. Assoc., Sci. Ed. 43*:159 (1954).
6. Belknap, E. L.: EDTA in the Treatment of Lead Poisoning, *Ind. Med. & Surg. 21*:305 (1952).
7. Belknap, E. L. and Perry, M. C.: Treatment of Inorganic Lead Poisoning with Edathamil Calcium Disodium, *A. M. A. Arch. Indust. Hyg. 10*:530 (1954).
8. Bessman, S. P. and Doorenbos, N. J.: Chelation, *Ann. Intern. Med. 47*:1036 (1957).
9. Bessman, S. P. and Layne, E. C.: The Distribution of Lead in Blood After Ca EDTA, *Am. J. Dis. Child. 89*:292 (1955).
10. Bessman, S. P., Reid, H., and Rubin, M.: Treatment of Lead Encephalopathy with Calcium Disodium Versenate; Report of Case, *Med. Ann. Dist. of Columbia 21*:312 (1952).
11. Bessman, S. P., Rubin, M., and Leikin, S.: The Treatment of Lead Encephalopathy: A Method for the Removal of Lead During the Acute Stage, *Pediatrics 14*:201 (1954).
12. Breinin, G. M. and Devoe, A. G.: Chelation of Calcium with Edathamil Calcium Disodium in Band Keratopathy and Corneal Affections, *Arch. Ophthamol. 52*:846 (1954).
13. Chain, E., Philpot, F. J. and Callow, D.: Catalytic Effect of Metal Ions on Alcoholysis of the Penicillins, *Arch. Biochem. 18*:171 (1948).
14. Chenoweth, M. B.: Chelation as a Mechanism of Pharmacological Action, *Pharmacol. Rev. 8*:57 (1956).
15. Cotter, L. H.: Treatment of Cadmium Poisoning with Edathamil Calcium Disodium, *J. Am. Med. Assoc. 166*:735 (1958).
16. Cohn, S. H. and Gong, J. K.: Effect of Chemical Agents on Skeletal Content and Excretion of Injected Strontium, *Proc. Soc. Exper. & Biol. Med. 83*:550 (1953).
17. Cohn, S. H., Gong, J. K., and Fishler, M. C.: Ethylenediamine Tetraacetic Acid (EDTA) Treatment of Internal Radioactive Contamination, *Nucleonics 11*:56 (1953).
18. Cotter, L. H.: Treatment of Lead Poisoning by Chelation, *J. Am. Med. Assoc. 155*:906 (1954).
19. Dudley, H. C.: Influence of Chelates on the Metabolism of Radio-Yttrium (Y^{90}), *J. Lab. & Clin. Med. 45*:792 (1955).
20. Dudley, H. C., Ritchie, A. C., Shilling, A., and Baker, W. H.: Pathologic Changes Associated with the Use of Sodium Ethylene Diamine Tetra-acetate in the Treatment of Hypercalcemia, *New England J. Med. 252*:331 (1955).
21. Eisner, H. J., Stirn, F. E., Dornbush, A. C., and Olesan, J. J.: Enhancement of Serum Levels of Aureomycin in Experimental Animals, *J. Pharmacol. & Exper. Therap. 108*:442 (1953).
22. Everall, J. D. and Truter, E. V.: A New Approach to the Problem of Epidermal Contact Hypersensitivity, *A. M. A. Arch. Derm. 75*:428 (1957).
23. Figueroa, W. G. *et al.*: Effect of Disodium Calcium Versenate on Iron Excretion in Man, *Am. J. Med. 17*:101 (1954).
24. Foreman, H.: The Use of Chelating Agents for Accelerating Excretion of Radio-Elements, *J. Am. Pharm. Assoc., Sci. Ed. 42*:629 (1953).
25. Foreman, H., Finnegan, C., and Lushbaugh, C.: Nephrotoxic Hazard from Uncontrolled Edathamil Calcium Disodium Therapy, *J. Am. Med. Assoc. 160*:1042 (1956).
26. Foreman, H., Hardy, H. L., Shipman, T. L., and Belknap, E. L.: Use of Calcium Ethylenediamine Tetracetate in Cases of Lead Intoxication, *Arch. Indust. Hyg., 7*:148 (1953).
27. Foreman, H. and Trujillo, T. T.: The Metabolism of C^{14} Labeled Ethylenediamine Tetraacetic Acid in Human Beings, *J. Lab. & Clin. Med. 43*:566 (1954).
28. Foreman, H., Trujillo, T. T., Johnson, O., and Finnegan, C.: Ca EDTA and the Excretion of Plutonium, *Soc. Exper. Biol. & Med. 89*:339 (1955).
29. Foreman, H., Vier, M., and Magee, M.: The Metabolism of C^{14} Labeled Ethylene Diamine Tetraacetic Acid in the Rat, *J. Biol. Chem. 203*:1045 (1953).
30. Foye, W. O. *et al.*: Metal Chelates of Streptomycin, *J. Am. Pharm. Assoc. 44*:261 (1955).
31. Franklin, M., Rohse, W., Huerge, J., and Kemp, C.: Chelate Iron Therapy, *J. Am. Med. Assoc. 166*:1685 (1958).
32. Fried, J. F., Rosenthal, M. W., and Shubert, J.: Induced Accumulation of Citrate in Therapy of Experimental Lead Poisoning, *Proc. Soc. Exper. Biol. & Med. 92*:331 (1956).

33. Gehres, R. F., and Raymond, S.: A New Chemical Approach to the Solution of Urinary Calculi, *J. Urol. 65*:474 (1951).

34. Grant, W. M.: New Treatment of Calcific Corneal Opacities, *A.M.A. Arch. Ophthamol. 48*:681 (1952).

35. Griffenhagen, G. B., Pfisterer, J. L., and Sloth, S. K.: Assay of Pharmaceutical Tablets Containing Calcium by the Schwarzenbach Method, *J. Am. Pharm. Assoc., Sci. Ed. 40*:359 (1951).

36. Grob, D. and Johns, R. J.: Treatment of Anticholinesterase Intoxication with Oximes, *J. Am. Med. Assoc. 166*:1855 (1958).

37. Gubner, R. S. and Kallman, H.: Treatment of Digitalis Toxicity by Chelation of Serum Calcium, *Am. J. Med. Sci. 234*:136 (1957).

38. Hadley, G. G. and Larson, N. L.: Use of Sequestrene as an Anticoagulant, *Am. J. Clin. Path. 23*:613 (1953).

39. Hamilton, J. G. and Scott, K. G.: Effect of Calcium Salt of Versene upon Metabolism of Plutonium in the Rat, *Proc. Soc. Exper. Biol. & Med., 83*:301 (1953).

40. Hardy, H. L. *et al.*: Use of Monocalcium Disodium Ethylene Diamine Tetracetate in Lead Poisoning, *J. Am. Med. Assoc. 154*:1171 (1954).

41. Hirata, Y.: Experimental Diabetes, *Hukuoka Acta Med. 44*:23 (1953). Through *Chem. Abstr. 47*:9499e, 1953).

42. Holland, J. F., Danielson, E., and Sahagian-Edwards, A.: Use of Ethylene Diamine Tetraacetic Acid in Hypercalcemic Patients, *Proc. Sod. Exper. Biol & Med. 84*:359 (1953).

43. Ivermark, B. and Seldinger, S.: Damage in Rats from the Lead Salt of EDTA and from Umbradil, *Acta Rad. 48*:366 (1957).

44. Jaeger, H.: Stabilization of Aqueous Solutions of Ascorbic Acid, *Pharmazie 3*:536 (1948). (Through *Chem. Abstr. 43*:3972h, 1948).

45. Kadota, I. and Abe, T.: Chemical Specificity of Diabetogenic Action of Quinoline Derivatives, *J. Lab. & Clin. Med. 43*:375 (1954).

46. Karpinski, F. E. Jr., Rieders, F., and Girsh, L. S.: Calcium Disodium Versenate in Therapy of Lead Encephalopathy, *J. Ped. 42*:687 (1953).

47. Kissin, B. and Natelson, S.: Chelating Agents and Urinary Calculi, *Science 112*:367 (1950).

48. Kitzmiller, K. V., Cholak, J., and Kehoe, R. A.: Treatment of Organic Lead (tetraethyl) Intoxication with Edathamil Calcium Disodium, *Arch. Indust. Hyg. 10*:312 (1954).

49. Kneller, L. A., Uhl, H.S.M., and Brem, J.: Successful Calcium Disodium Ethylene Diamintetra-Acetate Treatment of Lead Poisoning in an Infant, *New England J. Med. 252*:338 (1955).

50. Maloof, C. C.: Use of Edathamil Calcium in Treatment of Chrome Ulcers of the Skin, *Arch. Indust. Health 11*:123 (1955).

51. Martell, A. E. and Calvin, M.: *Chemistry of the Metal Chelate Compounds,* Prentice-Hall, New York (1952).

52. Mattocks, A. M. and Hernandez, H. R.: Assay of Official Calcium Products by the Schwarzenbach Method. *J. Am. Pharm. Assoc., Sci. Ed., 39*:519 (1950).

53. Mitchell, W. G.: Antagonism of Toxicity of Vanadium by Ethylene Diamine Tetraacetice Acid in Mice, *Proc. Soc. Exper. Biol. & Med. 83*:346 (1953).

54. Moskowitz, M.: Mode of Action of Chelates in Protection Against *Clostridium perfringens* Toxin, *Nature,* (London) *181*:550 (1958).

55. Perry, H. M. and Schroeder, H. A.: Lesions Resembling Vitamin B Complex Deficiency and Urinary Loss of Zinc Produced by Ethylenediamine Tetraacetate, *Am. J. Med. 22*:168 (1957).

56. Peters, H. A., Eichman, P. and Reese, H. H.: Therapy of Acute, Chronic, and Mixed Hepatic Porphyria Patients with Chelating Agents, *Neurology 8*:621 (1958).

57. Peters, H. A., Woods, S., Eichman, P., and Reese, H. H.: The Treatment of Acute Porphyria with Chelating Agents: A Report of 21 Cases, *Ann. Intern. Med. 47*:889 (1957).

58. Popovici, A., Geschikter, C. F., Reinovsky, A. and Rubin, M.: Experimental Control of Serum Calcium Levels *in vivo, Proc. Exper. Biol. & Med. 74*:415 (1950).

59. Raymond, S. and Gehres, R. F.: Ethylenedinitrilotetraacetic Acid as a Solvent for Urinary Calculi, *Proc Soc. Exper. Biol. & Med. 74*:715 (1950).

60. Rubin, M., Gignac, S., Bessman, S. P., and Belknap, E. L.: Enhancement of Lead Excretion in Humans by Disodium Calcium Ethylenediamine Tetraacetate, *Science, 117*:659 (1953).

61. Rukavina, J. G. *et al.*: Schleroderma: Treatment of Three Cases of the Non-Calcific Variety by Chelation (EDTA), *J. Invest. Derm. 29*:273 (1957).

62. Sapeika, N.: Antagonism of Digitalis Action by Ethylene Diamine Tetraacetic Acid, *Arch. Internat. Pharmacodyn. 97*:373 (1954).

63. Sapeika, N.: Lead EDTA Complex. A Water Soluble Contrast Medium, *South African Med. J. 28*:759 (1954).

64. Schmidt, C. H., Hane, M. E., and Gomez, D. C.: A New Anticoagulant for Laboratory Procedures, A Comparative Study, *U. S. Armed Forces Med. J., 4*:1556 (1953). (Through *Chem. Abstr. 48*:791h, 1953).

65. Seeberg, V. P., Hidalgo, J., and Wilken, W.: Hemoglobin Regeneration Following Oral Administration of Chelated Iron. *Science 119*:608 (1954).

66. Seven, M. J. *et al.*: N-Hydroxyethylethylenediamine Triacetic Acid, Verenol, in the Treatment of Hemochromotosis, *Am. J. Med. Sci. 228*:646 (1954).

67. Shapiro, R.: Chelation in Contrast Roentgenography with Special Reference to Lead Disodium Ethylenediaminetetraacetic Acid (EDTA) *Am. J. Roentgenol. 76*:161 (1956).

68. Sidbury, J. B., Bynum, J. C., and Fetz, L. L.: Effect of Chelating Agent on Urinary Lead Excretion. Comparison of Oral and Intravenous Administration, *Proc. Soc. Exper. Biol. & Med. 82*:226 (1953).

69. Smith, V. H.: Removal of Internally Deposited Plutonium, *Nature* (London) *181*:1792 (1958).

70. Spencer, H., Vankinscott, V., Lewin, I., and Laszlo, D.: Removal of Calcium in Man by Ethylenediamine Tetraacetic Acid. A Metabolic Study, *J. Clin. Invest. 31*:1023 (1952).

71. Stocken, I. and Thompson, R.H.S.: Reactions of British Anti-Lewisite with Arsenic and Other Metals in Living Systems, *Physiol. Rev. 29*:168 (1949).

72. Swallow, W.: Solutions of Crystalline Penicillin, *Pharm. J. 168*:467 (1952).

73. Teisinger, J., Lustinec, K., and Srhova, J.: Effects of EDTA Calcium Disodium on Retention of Lead in the Liver, *Arch. Indust. Med. 17*:302 (1958).

74. Teisinger, J., Zumanova, R., and Zezula, I.: Effect of Edathamil Calcium Disodium on the Lead Content of Red Blood Cells and Blood Proteins, *Arch. Indust. Med., 17*:295 (1958).

75. Walshe, J. M.: Penicillamine, a New Oral Therapy for Wilson's Disease, *Am. J. Med. 21*:487 (1956).

76. Weinberg, E. D.: The Mutual Effects of Antimicrobial Compounds and Metallic Cations, *Bact. Rev. 21*:46 (1957).

77. Will, J. J. and Vilter, R. W.: A Study of the Absorption and Utilization of an Iron Chelate in Iron-Deficient Patients, *J. Lab. & Clin. Med. 44*:499 (1954).

78. Wittgenstein, A. M.: Disodium Ethylene Diamine Tetracetate. An Anticoagulant for Routine Hematological Work, *Am. J. Med. Technol. 19*:59 (1953).

79. Zucker, M. B.: Some Effects of Ethylene-Diaminotetracete (EDTA) on Blood Coagulation, *Am. J. Clin. Path. 24*:39 (1954).

EVALUTION OF A PHARMACEUTICAL SERVICE IN HOSPITALS

by GEORGE F. ARCHAMBAULT

► HOW "GOOD" IS YOUR PHARMACEUTICAL SERVICE? What is the opinion of your administrator, your clinicians, and the patients of your pharmaceutical service? How would your hospital pharmacy score under the critical eye of an experienced hospital pharmacist trained to evaluate pharmaceutical services in hospitals? Could he help you do your job better? Want to find out? Take the Minimum Standard for Pharmacies, the Pharmacy Elements of the Joint Commission on the Accreditation of Hospitals, the statements issued by the American Hospital Association on pharmacy practice in hospitals such as the statement or principles relative to the use of investigational drugs and the hospital—wise utilization of pharmacists; the Point Rating System developed by the Catholic Hospital Association; and if you have an internship, take the Minimum Standard for Pharmacy Internships in Hospitals and check yourself on all the points listed. Then check your operation against the Pharmacy Laws and Regulations of your state, against your State Food and Drug Laws and Regulations, your State Public Health and Hospital Licensing Laws and Regulations. Then you will but need to check through the Federal Narcotic and Alcohol Laws and Regulations to have covered most of the pertinent material. But these are not quite all the considerations for the *kind* of pharmacy you operate is not revealed nor is the competency of your department in handling patients and others revealed in checking your operation solely against these standards.

Management Tools

Let's go all the way and see if there is some tool of management that will let us audit ourselves further. Over the past decade many hospital pharmacists have asked me this question: "How can you tell whether a pharmacy is well managed or not?" My reply is usually the same—the job of the Chief of the Pharmacy Branch is to insure good pharmaceutical service in Public Health Service hospitals. To accomplish this, three things are required: (1) The development of a program and policies which, if properly implemented, will produce the desired results—excellent pharmacy service; (2) The implementation of the program and policies in each hospital pharmacy and the building of enthusiasm and interest in each chief and staff pharmacist to better this level of minimum performance; and lastly, (3) with the chief of a pharmacy service, pause two to three full days, every year or so, and audit with him his entire operation. In the audit, we note not only the weak points in his program but also the excellent and superb activities.

It is this last step that I wish to discuss with you today. The audit, "the pause that stimulates," this "examination of conscience"—if you will, that we use with each chief pharmacist in reviewing the program for which he is responsible.

Evaluation Study

First, one must understand that such an evaluation study is not a "check up" or a "spy" job. Pharmacists who are chiefs of pharmaceutical services in hospitals are obviously leaders in their professional specialty. As such, they are keenly interested in their profession and in the management of their departments. The men insist that their departments be outstanding services. Like the physician or like the owner of a pharmacy, they welcome the visit of a consultant, a member of their profession, competent in the evaluation field, who comes on the scene periodically. They welcome one who reviews with them the total operation and who gives to them, their administrator and to Headquarters a "bill of health" and a "charter" under which to operate for the next two years. At the same time, this visit provides someone with whom the men can "talk shop," someone who brings to the scene methods others use to handle similar situations that are currently giving the operator trouble.

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Do you want to take a tour through your pharmacy on this basis and see what you find? There has been handed to you the survey form used in this evaluation work. Check your pharmacy and see if it's not a delightful experience. Remember, you're checking on how well you and your staff have actually implemented your program.

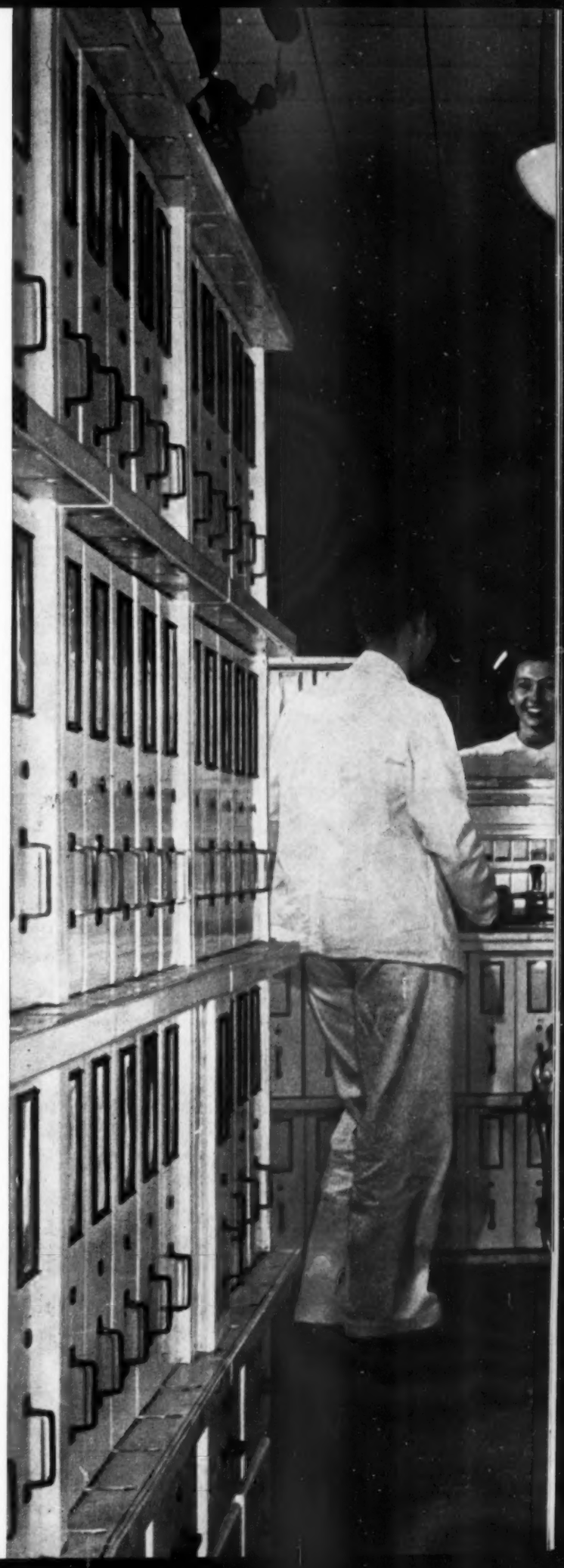
One new chief pharmacist coming up for his first review with me had this to say. "You know, Dr. Archambault, I could do this myself every six months. Why don't I?" The answer, I suspect, is simple. We become too involved, too busy with the routine, "with the trees" so to speak, to take time out to see "the forest." But let us be forced, or let us force ourselves to take two or three full days "off" each year to walk around our hospital with a check-off list such as the one you have just received, and we will usually be quite surprised at what we will find. A word of caution—do not sit at your desk and do this checking—you'll never find the skeletions in your department that way. Believe it or not, there are some there you don't suspect. Try it and see.

Some Areas of Evaluation

Time this morning prevents us from doing other than mentioning the contents of the evaluation form. Note, however, that it covers administrative items; intradepartmental relationships, activities and communications; physical layout, space and maintenance; supplies and equipment; narcotic and hypnotic control; staffing and workloads; and interdepartmental relationships and communications including formulary and pharmacy committee activities.

I'm sure you can improve the form to make it better fit your operation. We have used this technique for several years and find that it meets our needs nicely. Our chief pharmacists and medical officers-in-charge appreciate this type of an educational review. Our chiefs of services have copies of this evaluation report and know exactly what to expect when the service for which they are responsible is evaluated. The older men, in particular, enjoy the experience of the two or three day program review. They know its purpose —an educational tool, a management tool, to help them do their job better, and to emphasize the good jobs they are doing. As I stated before, real leaders welcome such a measuring tool of management, especially where they are responsible for a service employing several individuals. To those of you in civilian hospitals that deal with patient drug charges and with social workers—revise the analysis form to cover these essentials.

Make this two to three day analysis. You will be surprised and pleased with what you discover. It is an ideal "self evaluator," one that pin points for your administrator and for yourself, the effectiveness of the operation for which you are responsible.



FIELD STUDY REPORT

HOSPITAL_____ CLINIC_____

Evaluation made by Chief, Pharmacy Branch, Division of Hospitals, Washington, D. C. Date of Visit_____

► PURPOSE OF VISIT: To evaluate the Pharmaceutical Service for the benefit of Headquarters, the Medical Officer in Charge and the Chief of the Pharmaceutical Service at the station visited. This survey is made in an effort to aid the station in developing and maintaining an efficient and effective pharmaceutical service; one meeting in full the standards of the Joint Commission on the Accreditation of Hospitals, the stated principles involving pharmacy service and drug utilization in hospitals as recommended by the American Hospital Association, and the Minimum Standards of the Hospital Division of The American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, as approved by The American Medical Association and The American Hospital Association.

The Pharmacy Branch program as outlined in the Manual of Operations of the Division of Hospitals and subsequent memoranda and bulletins is used as the base for this evaluation study.

Observations, Evaluations and Conclusions:

Organization and Administration

1. Supervision
The Pharmaceutical Service is under the supervision of the Medical Officer in Charge ____, Deputy Medical Officer in Charge ____, Other ____.

2. Division Policy Relative to the Pharmacy Program - Availability of Regulations and Standards to Pharmacy Staff

a. Pharmacy Procedure Manual Yes ____ No ____.
b. Hospital Circular Memoranda and Bulletins and other policy material released subsequent to issuance of manual. These memos are filed by fiscal year Yes ____ No ____. They are arranged by Pharmacy Branch key numbers Yes ____ No ____. Cancelled numbers are marked "Cancelled" and are maintained in the same chronological file Yes ____ No ____.
c. Intern Guidance Manual and folder Yes ____ No ____.
d. Minimum Standard for Hospital Pharmacies Yes ____ No____.

3. Staffing Pattern and Organization Charts

a. Staffing Pattern Chart of Department is posted in the Pharmacy Yes ____ No ____.
b. Organization Chart is posted in Pharmacy Yes ____ No ____.

4. Hospital Policy on P.R.N. and Standing Orders (State and Give Source of Information)

For Narcotics _____
For Legend Drugs _____
For Others _____

5. Hospital Policy on Telephone or Oral Medication Orders

State

6. Policy on Automatic Stop Orders
State

7. Policy on Procurement of Drugs when Pharmacy is Closed
State

8. Is a periodic sampling made of patient charts (medical records) by medical members of Pharmacy Committee for detecting inconsistencies in medication prescribing (over medication as to number of drugs prescribed and continuance of drug beyond a reasonable period) with report of findings made at least once annually at staff meetings, identity of M.D.'s, Dentists and patients not revealed Yes ____ No ____

Intradepartmental Relationships, Activites and Communications

1. Generic versus Trade Names
a. Headquarters policy relative to labeling nursing station and other medication containers by generic name is in effect* Yes ____ No ____
b. Generic name-trade name table (A.Ph.A. Bulletin No. 102 or equivalent) is current and available at nursing stations Yes ____ No ____

2. Labels, Containers, etc. in General

a. Individual outpatient prescription labels are neatly typed, carry identification number, date, full name of patient, complete directions for use (signa), contents if requested and name of prescriber Yes ____ No ____
b. Outpatients receive prescription identification check form 1719 Yes ____ No ____
c. Each outpatient prescription is "filled" separately to insure accuracy Yes ____ No____
d. Medication containers (In and Outpatient) are air tight, light resistant, meeting standards of U.S.P. and N.F. Yes ____ No ____.

3. Dispensing Envelopes—Form Nos. PHS 1586-2, PHS 1586-1, PHS 1055, three sizes are available Yes ____ No ____

4. White Paper Bags—In use ____, Not in use ____. Should be used, (not the brown grocery store type bag).

5. Three sizes of White Wrapping Paper are Available on Special Roller Stand, String and Tape are Available Yes ____ No ____

6. Biologicals and Other Expiration—Dated Items

a. Division Control System (Form 1707) is in effect Yes ____ No ____
b. The monthly check is made and noted on Form 1707 with checker's signature and date Yes ____ No ____

*Policy where basic drug is on the market under more than one trade name, generic name only is used. Where basic drugs is controlled by one drug firm or where the station uses one brand only, the trade name may appear in brackets, directly beneath the generic name.

c. A check on these items revealed outdated stocks Yes ____ No ____.
d. Items found outdated with expiration dates:

Item	*Expiration Date*
(1)	
(2)	
(3) etc.	

e. Small Pox Points and Yellow Fever Vaccine are properly refrigerated at below zero temperature (in ice cube or deep freeze unit) Yes ____ No ____
f. Thermometers are kept in refrigerators Yes ____ No ____
g. Temperature of refrigerator was under 38 degrees F. Yes ____ No ____
h. Refrigerator is equipped with biological drawer inserts Yes ____ No ____
i. Items other than biologicals being refrigerated:
(1)
(2)
(3)
j. Refrigerator is of sufficient size Yes ____ No ____

7. Storage of Records—Prescriptions, Requisitions and Others

a. All records other than those on alcohol are neatly stored, readily available for a three year period and then destroyed with written permission of Medical Officer in Charge Yes ____ No ____
b. Talbot, Samuel or similar prescription files or microfilming are available for proper storage of "filled" prescription records Yes ____ No ____
c. Alcohol records are kept for a five year period Yes ____ No ____

8. Rubbing Alcohol and Cream Lotion

Both rubbing alcohol and a cream type lotion are available at nursing stations for back rubs Yes ____ No ____

9. Condition of Delivery Carts
Satisfactory ____
Need Replacement ____

10. Condition of Drug Baskets
Satisfactory ____
Need Replacement ____

11. Bulk Compounding
a. The Division's control system is in effect (Forms 1687, 1688) Yes ____ No ____
b. Forms not in proper use are:
(1). _____ (2). _____
c. A chronological log is maintained for bulk compounding activities Yes ____ No ____
d. Formulation Card (Form 1687) carries detailed compounding instructions Yes ____ No ____
e. Quantities bulk compounded are adequate in unit quantity compounded (wherever feasible not less than a minimum supply of one month should be bulk compounded) Yes ____ No ____
f. Items that should be compounded in larger quantities are:
(1)
(2)
(3) etc.
g. Macroscopical examination of solutions, lotions, ointments, creams and other preparations bulk compounded indicated preparations of good quality ____, average quality ____, poor quality ____. (Proper attention given to isotonicity, *p*H, filtration, sterilization, clarification, turbidity problems, humectants, surfactants, etc.). Items needing closer compounding attention are:
(1) Ointments gritty ____ Satisfactory ____
(2) Creams lumpy ____ Separated ____ Satisfactory ____
(3) Elixirs not brilliant ____ Sparkling ____ Satisfactory ____
(4)
(5) etc.
h. Items that should be purchases rather than bulk compounded are:
(1)
(2)
(3) etc.
i. Filtering equipment and supplies are adequate Yes ____ No ____
j. Homogenizing equipment available Yes ____ No ____
k. Suitable mechanical mixing equipment is available Yes ____ No ____

12. Antidotal Chart, Antidotal and Emergency Drug Cabinet, Clinical Toxicology Reference Material

a. Antidotal Charts are readily accessible to physicians Yes ____ No ____ Locations: 1. _____ 2. _____
b. Antidotal and Emergency Drug Cabinet is well stocked Yes ____ No ____
Additional items to be considered for inclusion:
(1)
(2)
(3) etc.
c. Clinical Toxicology Reference Material is available Yes ____ No ____
Describe:
d. Poison Information Control Center and telephone number are posted Yes ____ No ____
Center _____
Telephone _____
Not known _____

13. Prepackaging
a. Division control system for prepackaging is in effect (Forms 1686, 1309). Yes ____ No ____
b. Cost of each item prepackaged is shown on each Monarch Label Yes ____ No ____
c. Prepackaging forms not in proper use are _____
d. "Prepackaging," in addition to nursing station medication items, is utilized for the following stations outside the hospital:
(1)
(2)
(3) etc.
e. A chronological log is maintained for prepackaging activities Yes ____ No ____
f. Celons or cello-seals are used on prepackaged items, narcotics, hypnotics Yes ____ No ____
g. Prepackaged pharmaceuticals are obtained from Perry Point on Form 2510 (1056) Yes ____ No ____

14. Macroscopical Examination of Parenterals

a. Parenteral solutions are light tested and dated at time of issue from the Pharmacy Yes ____ No ____
b. Parenteral solutions are sent directly to nursing stations with an emergency supply kept at Central Sterile Supply Yes ____ No ____
c. Are sent to Central Sterile Supply for reissue Yes ____ No. ____
d. Emergency Supply at Central Supply is rotated monthly Yes ____ No ____
e. Supply at Central Sterile Supply is further light tested and dated at time of release rom Central Supply by nurse dispensing Yes ____ No ____

15. Intern Program
a. A pharmacy intern program is in operation Yes ____ No ____

b. Name of Intern _____ School _____
c. Comments relative to program:

d. Is U.S.P.H.S. Intern Guidance Manual being followed? Yes ____ No ____
e. Minimum Standard for Pharmacy Internships in Hospitals (of ASHP and A. Ph.A.) is being met Yes ____ No ____.
f. Status of program relative to surgery, medicine, nursing, administrative areas. Are intern observations made with medical and dental interns in routine ward rounds, etc. teaching activities? Yes ____ No ____
g. Areas deficient in (e) are:
(1)
(2)
(3) etc.

Physical Layout and Maintenance

1. Location (Ideal location is adjacent to outpatient department and in close proximity to elevators).

a. This pharmacy is located on ____ floor, _____

b. Location is satisfactory Yes ____ No ____

2. Space and Layout—Present square footage* of pharmacy is ____
a. Bed capacity of hospital is listed at ____ beds.
b. Average number of outpatient prescription daily ____ (not units).
c. Breakdown of square footage of present space is:

(1). Inpatient Dispension Area	____ sq. ft.
(2). Outpatient Dispensing Area	____ sq. ft.
(3). Bulk compounding Dispensing Area	____ sq. ft.
(4). Prepackaging Area	____ sq. ft.
(5). Storeroom Area	____ sq. ft.
(6). Office of Chief	____ sq. ft.
(7). Special Technique Area	____ sq. ft.
(8). Cool Room or Area	____ sq. ft.
(9). Other Areas	____ sq. ft.

d. Additional total square footage needed for minimum ASHP requirements ____ sq. ft.

Remarks:

3. Items checked are available—Air ____ Gas ____ Electric ____ Vacuum outlets (or pumps) ____

4. Fire Protection and Safety Provisions

a. Fire extinguishers are conveniently located Yes ____ No ____
b. Carbon tetrachloride extinguishers are employed (should not be used in confined areas) Yes ____ No ____
c. Date fire extinguishers were last checked_____
d. Fire blanket or emergency shower is available Yes ____ No ____ Specify type _____
e. Ether, alcohol and other highly volatile liquids are stored under conditions meeting standards of Federal and local fire regulations Yes ____ No ____
f. Explosion proof light and switch is installed in explosive and volatile liquid supply storage area Yes ____ No ____
g. Blow-out wall or window is present Yes ____ No ____
h. Floor drain Yes ____ No ____
i. Proper ventilation Yes ____ No ____
j. Other provisions such as raised door sill, etc. ____

5. Office or Desk Space for Chief Pharmacist

a. Well equipped Yes ____ No ____
b. Space is suitable for interviewing medical service representatives, pharmaceutical industry, clinical research (regional and national) directors, physicians, other staff members and others Yes ____ No ____

6. Storeroom

a. Adequate in size Yes ____ No ____
b. Properly ventilated and lighted Yes ____ No ____
c. Located close to pharmacy Yes ____ No ____
d. Open shelving Yes ____ No ____
e. Recommendations:

7. Solution Room or Area

a. Adequate in size Yes ____ No ____
b. Properly lighted and ventilated Yes ____No ____
c. Autoclave of proper size (24 x 36 x 48 inches—if heavy loads) Yes ____ No ____
d. Still of sufficient capacity with conductivity meter and Pyrex carboys Yes ____ No ____

8. General Appearance of Pharmacy

a. Neat, clean and tidy Yes____ No ____
b. Dirty, dusty, disorderly Yes ____ No ____
c. Proper waste receptacles (foot pedal operated top closures) have been provided Yes ____ No ____
d. Condition of fixtures—Good ____ Need refinishing ____ Need replacement ____
e. Fixture needs
(1) Condition of bench tops—Good ___ poor___
(2)
(3) etc.
f. Type of lighting in pharmacy _____
g. Type of flooring in pharmacy _____
h. Is pharmacy air conditioned ? Yes ____ No ____
i. Adequate facilities provided for storage of brooms, mops, buckets, waste, etc. Yes ____ No ____
j. Dutch door ____ Window ____ to pharmacy

Comments:

Supplies and Equipment

1. General Appearance of Storeroom

a. Neat, clean and orderly Yes ____ No ____
b. Dirty, dusty and disorderly Yes ____ No ____
c. Stock is properly "faced" on shelves Yes ____ No ____
d. Shelf stripping is in effect Yes ____ No ____
e. Stock is dated on receipt into stores Yes ____ No ____

2. Equipment Needs

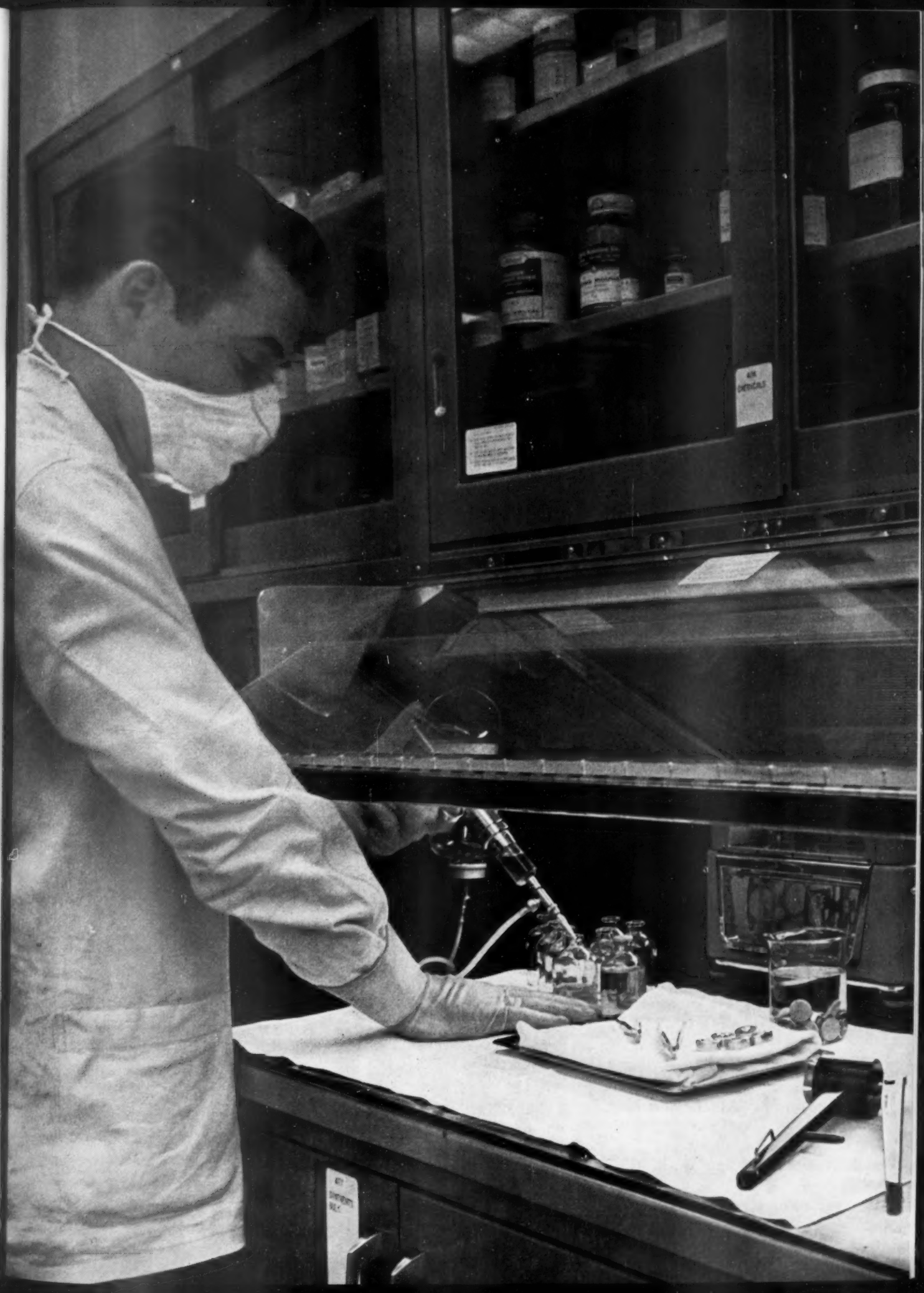
a.
b.
c. etc.

3. Small Item Equipment Needs

a. Filter paper supply is satisfactory (sizes and types) Yes ____ No ____
b. Weights satisfactory Yes____ No ____
c.
d.
e. etc.

4. Still
a. Type of still _____
b. Capacity per hour _____
c. Pyrex containers present Yes ____ No ____
d. Date still last cleaned _____
e. Conductivity meter present Yes ____ No ____
f. Silver Nitrite test indicated presence of chlorides Yes ____ No ____

*Average minimum square footage recommended by ASHP and Division of Hospital Facilities, USPHS, is 5 square feet per bed exclusive of storage space and other non-operating areas. British standards run higher.



5. A.Ph.A Sensitivity Test Chart for Checking Prescription Balances in Use Yes ____ No ____
Date Balances Last Checked _____

6. Pharmacy Storeroom Inventory

a. A ten item spot-check on physical stocks against the perpetual inventory records indicated an inventory record accuracy of ____%

Items	*Perp. Record Count*	*Phy. Count*
(1)		
(2)		
(3) etc.		

7. Stockturn—Usage Rate—Purchases

a. Stockturn last fiscal year was _____ indicating a _____ inventory (4.5 to 5.5 satisfactory)
b. Surplus or obsolete stock Yes ____ No ____ Estimated value _____
c. Number of items stocked _____ Value $ _____
d. Number of items non-moving in past year ____ Value $ _____
e. Value of stock issued last year $_____
f. Value of stock purchased last year $_____
g. Inventory increased ____ Decreased ____ last year by $ ____

Recommendations:

8. Pharmacy Inventory (not storeroom)

a. Inventory is light ____ heavy ____ average ____
b. Stock is dated Yes ____ No ____
c. Stock is in excess of pharmacy needs, should be surveyed and excess stock returned to storeroom Yes ____ No ____ Estimated value of excess stock $ ____
d. Drugs not in formulary are stocked Yes ____ No ____

Comments:

9. Texts and Journal Requirement

The following texts and journals are needed as working references:

a. *American Journal of Hospital Pharmacy* (formerly *The Bulletin*) (copies are bound each year) Yes ____ No ____.
b.
c. etc.

10. Narcotics

a. Morphine Tartrate Syrettes for Civilian Defense Security is:
Excellent—T-60 Safe _____
Good—T-20 Safe _____
Satisfactory _____
Poor _____

Comments:

b. Audit of narcotic reserves
(1) A five item spot-check of physical stocks against the perpetual inventory records indicated a balance accuracy of ____ %

Item	*Perp. Rec. Bal.*	*Phy. Stock Count*

(2) Spot-checks on narcotic controls
(a). A check on receipts to pharmacy stores against the numerically numbered narcotic service requisitions, including Perry Point orders kept at the supply office indicated:
No irregularities _____
Irregularities _____
(b). Check on official narcotic order forms against Pharmacy store entries indicated:
No irregularities _____
Irregularities _____
(c). Official narcotic order forms are received from Narcotic Bureau by:
Regular mail _____
Registered mail _____
(d). A check on issues to pharmacy stocks from pharmacy stores against the pharmacy narcotic issue records indicated:
No irregularities _____
Irregularities _____

Comments:

(e). Audit of narcotic working stocks (pharmacy proper)
A five item spot-check of physical shock items against the perpetual inventory records indicated an accuracy of _____ %

Item	*Perp. Inv. Bal.*	*Phy. Stock Count*

Comments:

(e)2 A spot-check of narcotic and hypnotic records (prescriptions, requisitions, and receipts) indicated:
No irregularities _____
Irregularities _____

Comments:

(f.) Last station audit of pharmacy controlled narcotics was made on _____ _____ by Dr. _____

Comments:

(g). Monthly narcotic inventory and usage rate report (Form 1604) is made and compared with previous reports by Chief Pharmacist and report presented to the Medical Officer in Charge or Clinical Director Yes____ No ____
(h). Security
Security on reserve narcotic stocks is:
Excellent—T-60 Safe _____
Good—T-20 Safe _____
Satisfactory _____
Unacceptable _____

Comments:

(i). Each empty narcotic or hypnotic container is returned to the pharmacy with a Certificate of Disposition of corresponding number Yes ____ No ____
(j). Pharmacy personnel date and sign each Certificate of Disposition on the date returned Yes ____ No ____
(k). The pharmacist filling a narcotic prescription writes his full signature and date across the face of the prescription when filled Yes ____ No ____
(l). Chief Pharmacist, as narcotic security officer of the hospital, audits quarterly narcotic and hypnotic records of the purchasing (supply) department (official narcotic order forms and Perry Point orders) against entries in pharmacy records and stores and report findings in writing to his supervisor Yes ____ No ____
(m) The closed system is used for injectables of narcotics and other volume use dose medications. Yes ____ No ____ (See Hospital Bulletin No. 57-139)

11. Federal, State, and local pharmacy and other (narcotic, hypnotic, alcohol, etc.) pertinent laws and regulations are complied with including those (State

and Public Health Service) regulations pertaining to minimum equipment and reference tests
Yes ____ No ____

12. Perry Point Supply Depot

a. Average number of days for receipt of order ____
b. Any "cutting" of orders Yes ____ No ____
c. Specific complaints, if any, on stock items received____
Quality _____ Price _____
Comments:

13. Label Supplies, Bottles, Jars, etc.

Supply is adequate Yes ____ No ____
Efficiency of automatic form procurement system is Good ____ Fair ____ Poor ____

14. Staffing and Workloads

a. Pharmacy
(1). Staff consists of:
List
(2). Minimum "safe" standards of staffing for a pharmacy of this size is: _____

_____

_____

(3). Professional Affiliation of Staff
All members of the staff are members of the national and local branches of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACIST: Yes ____ ____ No ____
Comments: including career planning for pharmacist officers—next assignment, plans for attendance at ASHP, A.H.A., Hospital Pharmacy Institutes, etc.
(4). Recent Publications of Pharmacy Personnel
Name *Paper* *Journal*
(5). Pivot Duties of Pharmacy Personnel
(a). This pharmacy is responsible for "pivot" pharmacy service at the following stations:
_____
_____
_____
(b). Pivot service as supplied by _____ hospital is ____ is not ____ satisfactory.
Comments:

f. Sub-professional personnel engage in activities that must by law be performed only by pharmacists
Yes ____ No ____
Comments:

g. Nursing station medication issue days are Monday, Wednesday and Friday Yes ____ No ____
h. Staff members serve on the following hospital committees:
(1).
(2).
(3). etc.

2. Workloads

Last Fiscal Year, the pharmacy workload at this station ran _____ items, (prescriptions and requisitions) broken down as follows:
Alcohol _____
Narcotic _____
Hypnotic _____
Regular _____
Total _____
Nursing station issues _____
Issues to outpatient clinics and others _____
Bulk Compounded Units _____
Prepackaged units _____
Total units processed _____
Total workload last quarterly report _____

In addition, the following non-measurable activities are engaged in unless otherwise noted: Consultations (including indoctrinations) with medical, dental and other staff members on drug therapy and pharmacy matters, teaching schedules (dental pharmacology review, pharmacy intern and extern teaching programs, current trends in drug therapy lectures to nursing staff) requisitioning of supplies, maintenance of perpetual inventory records, preparation of monthly and annual reports (work loads, usage rates, stockturns, drug costs, narcotic and hypnotic and investigational drug controls) also preparation of Pharmacy Committee Meeting Agendas, Minutes and Bulletins, and responsibility for drug monographs in connection with station formulary, attendance at executive staff, departmental, pharmacy and other meetings, clinical pharmaceutical research activities, indoctrination and training of pharmacy personnel, audit of outpatient office physician prescription charges, preparation of station pharmacy procedural manual, etc.

15. Basket Pickup and Delivery or "Drug Service on Wheels" Service Performed by
Pharmacy ____
Nursing ____
Other ____
Indicate Which:
Basket Service _____
"Drug on Wheels" _____
Comments:

16. Pharmacy Department Drug Literature File
An adequate up-to-date ready reference drug literature file is maintained by the Department Yes ____ No ____

Interdepartmental Relationships and Communications

1. Management
a. Chief Pharmacist is a member of Department Heads' Management Committee Yes ____ No ____
b. Conference with department heads indicates satisfactory working arrangements with the department Yes ____ No ____ If no, explain in detail :____
_____
_____

2. Finance Department
a. Chief Pharmacist checks on reasonableness of prices charged by community pharmacists filling prescriptions of physicians for O.P. office, and for designated physicians (current Veterans Administration Pricing Schedule is used for this purpose) Yes ____ No ____
b. Pharmacy operates on a quarterly or monthly budget Yes ____ No ____ Amount $_____
c. Drug usage rate reflects all pertinent "other objects" (08.1 class) considered as "drugs for medicine and vaccines" purposes - Blood, gases, etc. Yes ____ No ____ If not, estimated difference yearly _____
d. Current fund situation:
Comments:

3. Dental and Laboratory Department
a. Dental pharmacology lectures are presented to dental inters by pharmacist Yes ____ No ____
b. Dental drugs are obtained from pharmacy and are not purchased directly through the purchasing official Yes ____ No ____
c. Exceptions to Item 2 above: _____
_____
_____
d. Spray bottles at Dental chairs are in satisfactory condition Yes ____ No ____

e. Laboratory drugs, chemicals, reagents and stains are obtained from or through the pharmacy in accordance with Headquarter's directive Yes ____ No ____

f. Working inventory for pathology laboratory is normal Yes ____ No ____.

g. Working inventory for dental drug supplies is normal Yes ____ No ____

4. Nursing Service

a. Surgical, Irrigating and Small Volume Parenteral Fluids

(1). Prepared by Pharmacy ____ Nursing ____

(2). Additional flasks needed Yes ____ No ____

(3). Water sterilizers in O.R. are used as source of surgical and irrigating fluids Yes ____ No ____ Should not be used.

(4). Solutions prepared are Saline ____, Water ____, Boric Acid ____, Other ____

(5). The Pathology laboratory checks on the sterility and pyrogenicity of parenteral solutions before release for use Yes ____ No ____

(6). Quantitative assays are performed to insure labeled strength of small volume parenterals Yes ____ No ____

b. Monthly Pharmacy-Nursing Audits of Nursing Station Medication Units

(1). Last station audit was made on _____

(2). Director of Nursing and Chief Pharmacist participated Yes ____ No ____

Comments:

(3). Written report of findings is made to Clinical Director or Medical Officer in Charge Yes ____ No ____

c. Nursing station medications are ordered on drug requisition (Form 1708) or station prepared form Yes ____ No ____

d. Inspection of Nursing station medication cabinets with nursing and pharmacy personnel indicated:

(1). Myotic, mydriatic, astringent and similar solutions carry expiration dated labels Yes ____ No ____

(2). Out-dated stocks were noted Yes ____ No ____

(3). Spray bottles at E.E.N.T. chairs were is satisfactory condition Yes ____ No ____

(4). Nursing station medication cabinets were found locked Yes ____ No ____

(5). Medications are prepared by Nursing Services several hours in advance of need Yes ____ No ____ (Should not be prepared in advance)

e. Hypnotics and narcotic controls at nursing stations:

(1). Spot-checks indicate proper balances of physical stocks to records Yes ____ No ____

(2). Narcotic and Hypnotic, etc. Certificates of Disposition were found outstanding longer than 45 days without re-issue Yes ____ No ____

f. Nursing station medication containers and labels:

(1). System Used:

(a). Type:
Prepackaged ____
Dual Container system ____
Mixed system ____

(b). Nursing station medication container sets need replacing and label standardization Yes ____ No ____

(2). Labels

(a). Neat Yes ____ No ____

(b). Need renewing Yes ____ No ____

(c). Standard height on containers Yes ____ No ____

(d). Shellac or label protective used Yes ____ No ____

(3). Violations of check-out-check-in eight hour nursing audit were noted Yes ____ No ____

g. An annual (or more often) lecture is presented to nursing staff by Chief Pharmacist on newer drug therapy agents Yes ____ No ____

h. Label changing by nursing personnel was noted Yes ____ No ____

i. Medication cabinets are adequate to needs Yes ____ No ____

j. Medication cabinets are provided with interior lights Yes ____ No ____

k. Externals and poisons are separated from internal medications Yes ____ No ____

l. Cocaine solution is properly controlled (legally) in O.R. Yes ____ No ____. In E.E.N.T. Yes ____ No ____

m. Space saving airtight light resistant medication containers are employed where feasible on nursing station medication centers Yes ____ No ____

n. Medication containers are dated and coded Yes ____ No ____.

o. Nursing station medication inventories are excessive ____ in short supply ____ satisfactory ____.

Comments:

5. Physician and Patient Relationships

a. Conferences with chiefs of services (medical, surgical, dental, etc.) indicate satisfaction with the department Yes ____ No ____ If no, explain in detail

_____

b. Prescription writing, quantities, signas, code, number and trade-name writing:

(1). A spot-check of recent prescriptions indicated unusual quantity or "refill number" type prescribing Yes ____ No ____

Comments:

(2). Generic names used in prescribing Yes ____ No ____

(3). Improper signas such as "use as directed," "as prescribed" Yes ____ No ____

(4) Abuses in narcotic and hypnotic writing were noted Yes ____ No ____

(5) Pharmacists record manufacturer's name and lot control number on each prescription filled Yes ____ No ____

(6) Special gothic type keyboard typewriter is used for prescription and house order labels Yes ____ No ____

(7) Initials of pharmacist filling prescription recorded on prescription Yes ____ No ____

(8) A single prescription is filled at a time Yes ____ No ____

c. Violation of ethics in patient contact and prescription dispensing by pharmacists:

(1) Pharmacist, without consulting prescriber, cuts back on amounts prescribed Yes ____ No ____

(2) Pharmacist criticizes physician prescription to patient Yes ____ No ____

Comments:

6. Housekeeping and Laundry Department

a. Adequate security is maintained over cleansing agents kept in patient areas to prevent accidents or intentional swallowing of poisons, etc. Yes ____ No ____

b. Pharmacy furnishes and labels supplies in this area when stocks are obtained from pharmacy Yes ____ No ____.

7. Supply Activities

Headquarters approved Kardex "Purchase Card" system is used in requisitioning drugs Yes ____ No ____

The Supply Officer periodically (at least quarterly)

checks pharmacy stores physical stock count against the perpetual Inventory Record Yes ____ No ____ also use of investigational drugs

8. Dietetic Department

Flavoring extracts are furnished by pharmacy Yes ____ No ____ Name ____, ____, ____ ,____.

Vitamins, essential amino acid, mineral food supplements, sugar substitutes, oils, salt substitutes etc. are furnished by pharmacy as directed by Headquarters (H.C. Memo No. 53-164) Yes ____ No ____

9. Pharmacy Committee Activities

a. Number of Pharmacy Committee meetings held last fiscal year ____

b. Minutes of last two years are kept by the Pharmacist-Secretary in a neat, chronologically arranged file, available for inspection by Joint Commission on Accreditation surveyors and others Yes ____ No ____

c. Committee membership consists of:

d. Nursing and lay officials such as administrative officers attend committee meetings but do not vote Yes ____ No ____

Comments:

10. Status of Station Formulary (American Hospital Formulary Service ASHP)

a. Kept current Yes ____ No ____

b. Copies at Outpatient Clinics where prepackaged items are sent Yes ____ No ____

c. Copies at key points in hospital Yes ____ No ____

d. Recently added drugs including those not as yet in ASHP Supplements carry the six month date review notation Yes ____ No ____

e. Number of drugs added last year ____ Number of drugs on inventory ____ Number dropped last year ____

11. Staff Orientation Towards Division Policy of Drug Evaluation, Selection and Utilization and Control—also use of investigational drugs

a. Discussions with medical, dental, nursing and pharmacy personnel indicates a good understanding Yes ____ No ____

Comments:

b. Nurses at nursing stations using "investigational drugs" are instructed by Chief Pharmacist (as Secretary of Pharmacy Committee), on dosage, side effects, contraindications and clinical characteristics of drugs Yes ____ No ____

c. Investigational drugs are stored and issued by pharmacy Yes ____ No ____

d. Concensus of medical staff is that the pharmacists function well as drug therapy consultants—handle telephone and personal visits satisfactorily relative to drug size, strength, dosage calculations, specific uses, side effects, and contraindications of medications Yes ____ No ____

Comments:

e. Station policy requires separation of external use and poison medications from internal use drugs stocked in pharmacy Yes ____ No ____

f. Items such as sodium nitrite, oxalic acid, boric acid, isopropyl alcohol, and ammonia water located in the pharmacy proper are clearly labeled and properly isolated from internal use medications Yes ____ No ____

g. The station Operation Manual contains a pharmacy section Yes ____ No ____

Comments:

12. Station Policy on Physician Samples, Drug Displays and Medical Service Representative Interviews

a. Drug samples are given to patients only through the pharmacy on prescription or house order Yes ____ No ____

b. "Detail men" first call at the pharmacy Yes ____ No ____ Exhibits are arranged by the Chief Pharmacist and the Chairman of the Pharmacy Committee in accordance with station policy on exhibits (time, place, etc.) Yes ____ No ____

13. Program Review with Nursing Staff

This survey included a program review with the nursing staff Yes ____ No ____ Items covered in conference with nursing personnel were:

14. Supply - Pharmacy - Availability of Forms

The following forms checked are stocked for pharmacy use: (Information verified by Forms Clearance Officer).

No.	*Rev.*	*Name*	*No. Issued Last 24 Months*
583		Prescription Blanks	
1055		White Dispensing Envelope	
1308		Daily Work Sheet	
1309		Chronological Log—Prepackaging	
1310-1		Quarterly Report	
1310–2		Annual Report	
1435–1		Narcotic—Hypnotic, etc. Requisition	
1435–2		Certificate of Disposition for Narcotics, Hypnotics, etc.	
1435–3		Emergency Transfer	
1586–1		White Dispensing Envelope	
1586–2		White Dispensing Envelope	
1603		Monthly Narcotic Audit Report	
1604		Monthly Narcotic Report	
1605		Pharmacy Stores—Perpetual Inventory	
1606		Pharmacy—Perpetual Inventory	
1686		Prepackaged Item Control	
1687		Formulation Control Cards—Bulk Compounding	
1688		Bulk Compounding Work Sheet	
1689		Request for Non-Basic Drugs	
1707		Biological Expiration Control Form	
1708		Nursing Station Medication Orders	
2023	4/53	Purchase Request	
5708		Pharmacy Requisition	
HD–1A		Purchase Card and Experience Card	
HD–2	10/46	Stock Record Card	
HD–2A		Title Insert Form	

Is Chief Pharmacist consulted relative to annual requirement of each form by Forms Clearance Officer in accordance with Circular Memorandum No. 5753 Yes ____ No ____

15. Supervision of Central Sterile Supply is under Nursing _____ Pharmacy _____ Pathology _____

16. Radioactive Medications—who procures ?_____ What responsibility has Pharmacy in this area?

17. Comments of Director of Pharmacy Service of status relative to his department and its relationships with other areas of the hospital.

*Status of Recommendations Made by Chief, Pharmacy Branch, as Results of His Last Visit. Date*_____.

For Recommendations Based on This Survey see Summary Station Report of Similar Date.

WATER WASHABLE VEHICLES

by JOHN M. KNOX, M. A. EVERETT *and* A. C. CURTIS

► ANY TOPICAL VEHICLE CAN NOW BE RENDERED water washable with the incorporation of a properly selected surface active agent. Specific formulations were first introduced in a scientific exhibit at the American Academy of Dermatology in 1954,[1] but at that time no comments could be made as to the therapeutic effectiveness of these preparations. The compounding of water washable vehicles is not difficult. An oil-soluble surfactant such as Triton X-45 or Igepal 400* is added to the usual formulation at a concentration that is determined by the amount of oily material in the formula. The optimal concentration is usually 10 percent of the quantity of oil in the vehicle. Therefore, Lassar's paste, which is 50 percent petrolatum and 50 percent solids, needs approximately 5 percent of Triton X-45 or Igepal 400. Petrolatum alone requires a coupling agent in addition to the surface active agent before becoming completely water washable. A satisfactory agent is oleic acid which is employed in a concentration equal to that of the surfactant. A pharmacist may discover that slight modifications of the above recommendations may improve his vehicles in appearance, stability or consistency.

Increased Patient Acceptability

For the last four years various water washable formulations have been used in the treatment of routine dermatologic conditions on inpatients and outpatients; and after studying these vehicles, often in paired comparison evaluations, a few impressions have been obtained. No definite therapeutic advantages were found for the water washable vehicles over the regular vehicles; however, the incorporation of a surface active agent simplifies removal, improves the appearance of most formulations, and increases the ease and smoothness of application. In the paired comparison studies, patients often expressed a preference for the water washable vehicle. These preparations were therefore superior from a standpoint of utilization and patient acceptability.

Ease of Removal

Zinc oxide paste (Lassar's), zinc oxide ointment, petrolatum, cold cream, and liniments were included in the evaluations. Perhaps the most improved of all the vehicles is zinc oxide paste (Lassar's). Zinc oxide ointment, although similarly improved, is usually applied in a thin layer and removal is not such a problem. Cold creams can be formulated so that they are as easily removed as the vanishing creams which have been termed "water washable bases." Because powder collects on crust and exudate, the caking that occurs with the use of regular calamine liniment and Schamberg's Lotion is decreased but not entirely eliminated by the use of a water washable formulation. The oily component of a liniment can be completely removed by rinsing with tap water.

Most conditions warranting the use of petrolatum need lubrication; therefore, it is questionable if washable petrolatum is a significant advantage in many instances. However, when it is necessary to remove

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*These agents are alkyl aryl polyether alcohols. Tritons may be obtained from Rohm and Haas Co., Washington Square, Philadelphia, Pa., and Igepals from Antara Chemicals Division, General Aniline and Film Corp., 435 Hudson Street, New York City, New York.

petrolatum prior to dressing, washability becomes important. Messy preparations also become more acceptable; for example, the discoloration from 5 percent crude coal tar in petrolatum can be removed rapidly and effectively without soap or trauma. In addition, washable petrolatum is probably indicated when patients are taking therapeutic baths because the occlusive film disappears promptly to allow maximum benefit from the bath.

Comment

There has been no known incidence of contact epidermal sensitization, although in rare instances primary irritation was observed that could be attributed to inclusion of the surface active agent. This was usually seen in patients with subacute or acute dermatitis. In general, these reactions could be avoided by selecting a more drying and less oily vehicle. These reactions were infrequent and usually avoidable, thus we felt they were not a contraindication to using the improved formulations.

Water washable vehicles have been found to be advantageous enough to justify their being adopted as standard items. Therefore, these preparations are now routine vehicles in hospital formularies and pharmacies of the University of Michigan and the Texas Medical Center.

Summary

During the past four years, water washable vehicles have been used extensively in the treatment of dermatologic inpatients and outpatients. Their value is such that they have now become standard preparations in hospital formularies and pharmacies of two large university medical centers. Water washability does not appear to enhance therapeutic qualities of the vehicle; the chief advantages are ease of removal and patient acceptance.

Reference

1. Knox, J. M.; Everett, M. A.; and Curtis, A. C.: New Uses for Surface Active Agents, *Arch. Dermat.* Dec. 1956.

USEFULNESS OF AN EMERGENCY ANTIDOTE CABINET

by BERNARD SHLEIEN

► WITH THE GREATER AVAILABILITY OF DRUGS AND synthetic organic chemical products to the general public, each individual hospital is faced with an ever growing problem. Accidental poisoning, especially in younger age groups, continues to increase throughout the nation. In the year 1950 12,000 persons died from accidental and intentional exposure to harmful chemicals.[1]

By far, easy access to poisonous materials, especially drugs, contributed greatly to a death rate from accidental poisoning of 3.6 per 100,000 for the United States during the past decade.[2] Drugs and "materials for external use" accounted for the greatest portion of these poisonings, causing 33 and 36 percent, respectively. Petroleum products ran a close third. According to B. E. Conley, Ph.D., the major cause of poisoning in the drug group was due to salicylates, followed by barbiturates, bromides, and opium derivatives in a declining order.[1]

Children constitute the largest group of individuals prone to accidental poisoning, due to obvious reasons. In the 1956 report of the Seattle Poison Control Center the age distribution was as follows:[3]

7 months	to 12 months	40	5 years to 10 years	40
1 year	to 3 years	298	10 years to 14 years	16
3 year	to 4 years	149	Adults	30
4 year	to 5 years	80	Ages not reported	50

A further breakdown of causative agents in poisonings for this local area mirrors other industrial cities throughout the United States. Drugs again accounted for the greatest number of poisonings in children.[3]

Aspirin	111	Phenobarbital	7
Cough Syrup	19	Dextro amphetamine	7
Thyroid	10		

Ingested hydrocarbons ran a close second, followed by rodenticides and insecticides, plants and berries, caustics and corrosives, and bleaches.

Need Highlighted

The need for readily available toxicological information and available antidotes was highlighted at this hospital by the admission of two patients with visible effects of barbiturate overdosage. Also, during January a small child was seen in the outpatient department after she had ingested a quantity of household deodorizing solution. In the latter case the Pharmacy was able to provide useful information and further assist the physician with information regarding the Seattle Poison Control Center. Medical records show that this hospital has been called upon to treat poisonings and reactions from a great variety of substances during the past two years. A breakdown of poisonings is as follows:[4]

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Alcohol	45	Lead and Its Compounds	1
Petroleum Products	2	Gases and Vapors	4
Industrial Solvents	1	Barbiturates	6
Corrosives and Caustics	3	Aspirin and Salicylates	1

Besides the above, adverse reactions requiring treatment occurred with the following drugs:[4] Pantopaque, digitalis, chlorpromazine, penicillin, sulfisoxazole, scopolamine, opiates, chlortrianisene, anticoagulants, and pentolinium. While information, antidotes, and emergency equipment were available, their locations were scattered and thus a chance that treatment would be delayed arose. It is the function of the "Emergency Cabinet" to provide all the above facilities in a central location and in an efficient manner.

Emergency Antidote Cabinet

By no means should the emergency cabinet be considered on the same level as a Poison Control Center. Their functions are separate and distinct. While a Poison Control Center provides consultation service to all local physicians, and records, files and evaluates all poison cases reported in the area, it is the responsibility of the individual hospital to provide antidotes and facilities for the treatment of poison cases. Basic information provided in the emergency cabinet is intended for use by this hospital's staff only, and serves to provide even more rapid treatment than could be afforded by first contacting another agency.

Certainly, provisions should be made to contact the Poison Control Center, if the need arises and it is hoped that duplicate poison report forms will be forwarded to the Center.

The basic source of reference for the emergency cabinet is "The Toxicology of Commercial Products," by Gleason, Gosselin, and Hodge. The text is the combined efforts of a University of Rochester team and required five years for its completion. Over 4,500 manufacturers provided information concerning the toxicity of their products, and continue to do so in supplements which appear from time to time. The text presents, in a readily accessible fashion, information on the ingredients, toxicity, antidotes, and follow-up treatment of over 15,000 products. A flow sheet, a duplicate of which is present in the emergency cabinet, enables the physician to quickly obtain information. Three schemes are presented: 1. If the ingredients are known. 2. If the trade name is known. 3. If the trade name is unknown.

Table 1. Flow Sheet on use of "Clinical Toxicology of Commercial Products"

I.	If Ingredients Known	
	1. Section II	(Blue Section)
	2. Section III	(White Section)
II.	If Trade Name Known	
	1. Section V	(Yellow Section)
	2. Section II	(Blue Section)
	3. Section III	(White Section)
III.	If Trade Name Unknown	
	1. Section VI	(Second White Section)
	2. Section II	(Blue Section)
	3. Section III	(White Section)

Basic Philosophy

The basic philosophy in stocking the emergency cabinet was to provide antidotes for every procedure in "The Toxicology of Commercial Products." In some cases, in which a pharmacological group, such as the antacids, was suggested, the agent which afforded the most rapid action and least side effects was chosen. In other cases, several antidotes were suggested. For example, in barbiturate poisoning several analeptics can be used, or no analeptic therapy instituted. For this particular poisoning, the emergency cabinet is stocked with amphetamine sulfate injection, caffeine sodium benzoate injection, nikethamide injection, and picrotoxin injection. Thus, the physician is provided a choice of analeptics. An attempt was made to provide at least one specific antidote for each step in the treatment procedure and yet to allow the individual judgment of the physician and peculiarities of the case to determine measures to be taken.

A sufficient amount of each drug is stocked for treatment of the severest manifestations of any poisoning case. Antidotal solutions which must be freshly prepared are provided in the following manner. A weighed amount of the drug is placed in an empty container and a designated volume marked upon the container. In most cases these are lavage materials, and so tap water need only be added to the designated volume to prepare a fresh solution. In some cases, as with Universal Antidote, individual weighed doses are provided to preclude the need for any measuring prior to administration, and further to provide accurate dosages.

Arrangement

The antidotes are individually labeled and divided into four groups. 1. General 2. Injections 3. Lavage Fluids 4. I.V. Fluids. Each antidote is numbered and has a corresponding number on the stock sheet. Shelves containing each antidote are clearly labeled as to the group and antidotes therein contained.

The majority of equipment required to begin emergency procedure is stored in the emergency cabinet.

Table 2. Antidotes and Action

Acetic Acid 6%
a. Neutralization of alkaline agents in internal poisoning.
b. 1 x 500 ml.

Aluminum Hydroxide Gel
a. Used as antacid, demulcent and adsorbent in toxicities from acids, chlorinated propane-propylene mixtures, hypochlorite, and thallium.
b. 2 x 240 ml.

Aminophyllin Injection 0.25 Gm.
a. Correct bronchospasm in toxicities due to chlorinated propane-propylene mixtures.
b. 3 x 10 ml.

Ammonia Solution 0.2%
a. Conversion of formaldelyde to methenamine in internal poisoning of former.
b. 1 x 2000 ml.

Ammonia, Aromatic Spirit Ampuls
a. As above, and also as a mild stimulant.
b. 3 ampuls x 0.33 ml.

Amphetamine Sulfate Injection 20 mg.
a. Analeptic.
b. 6 x 1 ml.

Amyl Nitrite Perles 0.3 ml.
a. Rapidly converts hemoglobin to methemoglobin. The latter competes with cytochrome oxidase for the cyanide ion forming cyanmethemoglobin. This product is gradually reconverted to hemoglobin and relatively non-toxic thiocyanate ion.
b. 6 perles 0.3 ml.

Atropine Sulfate Injection 0.4 mg.
a. Used in poisoning due to cholinergic drugs such as pilocarpine, D.F.P., neostigmine, choline esters, and also in amanita, farium, digitalis, hydrogen sulfide, lead, nicotine and parathion.
b. 1 x 20 ml.

Caffeine-Sodium Benzoate 0.5 Gm.
a. Generally safe analeptic for wide range of poisonings due to CNS depressants. Remains effective for several hours. For example, required in higher alcohols, antihistamine, carbon disulfide, methanol, phenol, turpentine, and many other poisonings.
b. 6 x 2 ml.

Calcium Gluconate Injection 10%
a. Correction of hypocalcemia and inactivation of fluoride ion. Prevention of tetany in lead, benzene, hydrochloric acid and D.D.T. poisonings.
b. 3 x 10 ml.

Calcium Hydroxide Solution
a. Neutralizing agent in acid poisoning. Precipitation of toxic fluoride and oxalate ions.
b. 1 x 1000 ml.

Calcium Lactate Tablets 0.3 Gm.
a. Precipitation of insoluble calcium oxalate preventing absorption of toxic oxalate ion.
b. 1 x 100

Castor Oil
a. Oily cathartic for use where saline cathartics are contraindicated.
b. 1 x 120 ml.

Cupric Sulfate Solution 0.2%
a. Coats phosphorous particles with insoluble copper phosphide.
b. 1 x 500 ml.

Dimercaprol in Oil Injection 10%
a. Capable of preventing and reversing the inhibitory effect on sulfhydryl enzyme systems of toxic substances such as arsenic, cadmium, copper, mercury, methyl bromide, and thallium.
b. 10 x 4.5 ml.

Diphenhydramine Injection 10 mg./ml.
a. Useful in anaphylactic shock and allergic toxic manifestations.
b. 1 x 30 ml.

Edathamil Calcium Disodium Injection
a. Chelating agent used in lead poisoning.
b. 6 x 5 ml.

Ephedrine Sulfate Capsules 25 mg.
a. As an adjuvant in analeptic therapy with caffeine sodium benzoate.
b. 10

Epinephrine Injection 1:1000
a. Used in anaphylactoid reactions.
b. 4 x 1 ml.

Evaporated Milk
a. Demulcent.
b. 1 can

Gelatin Solution (20 Gm. for solution)
a. Demulcent in cadmium, morphine, and quaternary ammonium compound toxicities.
b. Calibrated container—q.s. with water to 500 ml.

Hydrocortisone I.V. 100 mg.
a. Shock-stress therapy.
b. 2 ampuls

Levallorphan Injection 1 mg.
a. Specific antagonist in opiate poisoning.
b. 3 x 1 ml.

Liquid Petrolatum
a. Demulcent in the treatment of acids, aliphatic thiocyanates, kerosene, phosphorous and xylene.
b. 500 ml.

Magnesia Magma
a. A non-saline and non-oily antacid and laxative used in toxicity due to hypochlorite, mercury and oxalate poisonings.
b. 240 ml.

Magnesium Sulfate
a. General saline cathartic. Specifically used in aniline poisoning.
b. 120 Gm.

Methylene Blue Injection 1%
a. Converts methemoglobin caused by aniline and nitrite poisonings to hemoglobin.
b. 2 x 20 ml.

Meperidine HCl Injection 50 mg./ml.
a. Narcotic analgesic.
b. 5 x 2 ml.

Morphine Sulfate Injection 10 mg./ml.
a. Narcotic analgesic.
b. 1 x 20 ml.

Mustard Powder
a. Emetic.
b. 120 Gm.

Nikethamide Injection 25%
a. Respiratory stimulant whose site of action is the chemoreceptor of the carotid bodies rather than the respiratory center itself.
b. 4 x 1.5 ml.

Nor-epinephrine Injection 0.2%
a. Vasopressor agent necessary in treatment of shock.
b. 10 x 4 ml.

Olive Oil
a. Oily demulcent suggested in acid, alkali, ammonia, and phenol poisonings.
b. 120 ml.

Paraldelyde
a. Anticonvulsant and sedative in atropine and salicylate poisonings.
b. 30 ml.

Pentobarbital Sodium Injection 5%
a. Intermediate acting barbiturate.
b. 3

Pentamethylenetetrazol 0.1 Gm.
a. Analeptic.
b. 6 x 1 ml.

Phenobarbital Sodium Injection 0.32 Gm. in Propylene Glycol
a. Long acting barbiturate.
b. 3

Phenylephrine Hcl Injection 10 mg.
a. Vasopressor agent.
b. 2 x 1 ml.

Picrotoxin Injection 3 mg./ml.
a. Analeptic.
b. 2 x 20 ml.

Pilocarpine Nitrate 5 mg.
a. Physiological antidote for atropine.
b. 10

Potassium Ferrocyanide 1% (10 Gm. for solution)
a. Forms insoluble copper ferrocyanide in poisoning due to cupric ingestion.
b. Calibrated container—q.s. with water to 1000 ml.

Potassium Iodide 1% (10 Gm. for solution)
a. Forms insoluble thallium iodide in thallium poisonings.
b. Calibrated container—q.s. with water to 1000 ml.

Potassium Permanganate 1:5000 (0.8 Gm. for solution)
a. For gastric lavage in poisoning due to amanita toxin, barbiturates, ethylene glycol, morphine, nitrite, phosphorous and strychnine.
b. Calibrated container—q.s. with water to 4000 ml.

Procainamide Injection 100 mg./ml.
a. Combat ventricular fibrillation in poisoning due to digitalis and fluoroacetate.
b. 2 x 10 ml.

Protamine Injection 1%
a. Specific antidote for heparin.
b. 3 x 5 ml.

Quinidine Sulfate 0.2 Gm.
a. Orally effective against ventricular fibrillation due to barium, 2-4-D, digitalis, and fluoroacetate.
b. 100

Sodium Ascorbate Injection 1 Gm.
a. Overcome methemaglobin in aniline and nitrite poisoning. Supportive therapy in disulfiram, warfarin and xylene toxicities.
b. 2 x 5 ml.

Sodium Bicarbonate Injection 3.75 Gm.
a. Supportive therapy in acidosis.
b. 2 x 50 ml.

Sodium Bicarbonate Solution 3 and 5% (120 Gm. for solution)
a. Gastric lavage in dinitrophenol, ethyl alcohol, kerosene, mercury, methanol, parathion, salicylate, and turpentine poisoning.
b. Calibrated container 3% q. s. with water to 4000 ml.
5% q. s. with water to 2400 ml.

Sodium Bicarbonate Powder
a. For external neutralization of acids.
b. 120 Gm.

Sodium Nitrite Injection 0.3 Gm.
a. See amyl nitrite.
b. 3 x 10 ml.

Sodium Phosphate
a. Cathartic.
b. 120 Gm.

Sodium Thiosulfate Injection 25%
a. Conversion of cyanide to thiocyanate said to be hastened by sodium thiosulfate.
b. 1 x 50 ml.

Sodium Thiosulfate 1% (40 Gm. for solution)
a. Gastric lavage in arsenic, bromide, and iodine poisoning. Reducing agent.
b. Calibrated container q. s. with water to 4000 ml.

Starch
a. Demulcent in poisoning due to complex formation with iodine.
b. 120 Gm.

Thiopental Injection 0.5 Gm.
a. Short-acting barbiturate.
b. 3

Tannic Acid
a. Alkaloidal precipitant.
b. 120 Gm.

Universal Antidote
a. Precipitant, adsorbent, neutralizer.
b. 15 Gm. pkg. No. 12.

Vitamin K_1
a. Combat hypothrombinemia in phosphorous and warfarin poisonings.
b. 3 x 50 mg.

For example, the opening tray for the Cardiac Resuscitation Kit is in the emergency cabinet, but the Cardiac Resuscitation Kit itself remains in Surgery where it is perhaps more often required and must be more readily available. Oxygen inhalation equipment, while not in the cabinet itself, is on a mobile unit and is kept in the Outpatient Department treatment room, next door. Certain equipment, such as a Pneumophore Positive Pressure Apparatus and Artificial Kidney, are not available at this hospital. A card giving information on how to obtain this equipment from local hospitals is posted on the door of the emergency cabinet.

The maintenance of the emergency cabinet is the responsibility of the Pharmacy, which maintains a monthly check on the condition of the cabinet and its contents. However, due to the fact that even if one antidote is missing from the emergency cabinet, the unit loses its usefulness, it is hoped that when an antidote is used it will be reported to the Pharmacy.

Although the emergency cabinet will only be used occasionally, it is by its very nature an important part of providing complete patient care. It is hoped that it will allow for greater efficiency and ease in treating poisonings, and more adequately round out those activities of this hospital which are inherently of an infrequent but life-saving nature.

References

1. Conley, B. E. Ph.D., *Am. J. Pharm.* 129:87 (Mar.) 1957.
2. Brain, K. M.D., *J. Pediat.* 44:616 (June) 1954.
3. Occupational Health News Letter March 1957.
4. Medical Records U.S.P.H.S. Hospital, Seattle, Wash.

Therapeutic Trends

edited by WILLIAM JOHNSON

Acne and Tolbutamide

Rapid recovery of moderately severe acne was found in two patients being treated with tolbutamide for diabetes. In view of this fact 23 other patients were given tolbutamide and carefully followed up. The conditions of the patients consisted of deep pustular acne chronic staphyloderma, recurrent furunculosis, sycosis vulgaris hidradentis suppurativa and other resistant pustular infections of the skin. Acne is still one of the greatest problems and the management of it is still the major activity of most dermatological practices. Tolbutamide had proved to be a good adjuvant for this treatment. The effects on acne patients are much better than those of the broad spectrum antibiotics and are obtained with a fraction of the cost. Of course the hypoglycemic effect is more marked in the diabetic than the normal individual. Routine checks on fasting blood sugar levels in several patients taking two 0.5 gram tablets every day were all within normal limits. A series of 26 patients with pustular acne vulgaris and other pustular dermatoses resistant to the usual forms of therapy were treated with 0.5 gram to 1.0 gram tolbutamide from one to four months, and all improved. In six patients the improvement was fair; the rest was good or excellent. One failure in a woman allergic to sulfonamides was observed. Cohen and Cohen report in *Canad. J. Med. 80*:629 (Apr.) 1959, that the results obtained so far warrant further broader investigation of the compound and its relationship to dermatological conditions. A 1.0 gram daily dosage lowers the blood sugar about 10 percent in normal individuals. The drug was supplied as Mobenol by Frank Horner Ltd.

RICHARD H. HARRISON

Phenazocine—A New Benzomorphan Narcotic Analgesic

Phenazocine was tested in clinical trial to evaluate its analgesic effectiveness. The study included 160 patients, both male and female. The reasons for use of an analgesic were postanasthetic restlessness, acute postoperative pain, and chronic pain. The dosage range was 0.5 mg. 1.5 mg. In some cases of chronic pain, the dose went as high as 2.5 mg. during the day, and 3 mg. at night. Some respiratory depression was noted and hypotension was also noted in a few patients. No nausea or vomiting was attributed to the drug. The side effects, although present, were in a very small percentage and of no clinical significance. Based on previous tests with other narcotics as postoperative analgesics, the new drug, phenazocine, appeared to be about ten times as potent as morphine. The potency seemed to be about seven times that of morphine in treating chronic pain. These tests also showed that there is a possibility of addiction. This study was made by Eckenhoff and the results are reported in *Anesthesiology 20*:355 (May-June) 1959. The drug was supplied as Prinadol by Smith, Kline, and French Laboritories.

RICHARD H. HARRISON

Nicoumalone—A New Anticoagulant

Nicoumalone, a new coumarin derivative was studied and compared with phenindione. In the *Brit. Med. J. 4*:1211 (May 9) 1959, favorable results are reported in the search for the ideal anticoagulant. Early results indicated that doses of 12 mg. on the first day and 6-8 mg. on the second day were sufficient to depress the "prothrombin" to the desired level, 20 percent activity. (Prothrombin time 39 seconds as compared with a control time of 13 seconds.) Maintenance doses varied but were generally 2-3 mg. daily given as a single evening dose. The occasional omission of a dose did not result in wide fluctuation of the prothrombin level, in the more sensitive patients. The withdrawal of the drug from patients receiving 2-4 mg. daily resulted in a return to normal with 36-48 hours. In very sensitive patients this period may be longer, while in some cases the return to normal required only 24 hours. In this study the stability of the prothrombin levels of 269 patients was compared with phenindione. The results seem to warrant further study of the new drug.

RICHARD H. HARRISON

Timely Drugs

Arthropan Liquid

GENERIC NAME: Choline salicylate.
INDICATIONS: Anti-arthritic, anti-inflammatory analgesic, absorbed 5 times more rapidly than aspirin and reaching a peak blood level 12 times more rapidly; indicated in various types of arthritis, rheumatic fever, bursitis, neuralgias, myositis, fibrositis, and other musculoskeletal disorders associated with pain.
DOSAGE: As directed by physician.
PREPARATIONS: Cherry-flavored liquid containing in each 5 ml. choline salicylate 0.87 Gm. (equivalent to 0.6 Gm. aspirin).
PACKAGING: Bottles of 8 and 16 ounces.
SUPPLIER: Purdue Frederick Co.

Casakol

COMPOSITION: Poloxalkol (Polykol) and casanthranol, an active constituent of cascara sagrada.
INDICATIONS: For the treatment of chronic constipation and for re-establishing a normal bowel habit.
DOSAGE: Adults, 1 or 2 capsules or 1 or 2 teaspoonfuls of syrup, taken at bedtime. Children, 6 to 12 years of age, 1 capsule or 1 teaspoonful of syrup, at bedtime.
PREPARATIONS: Capsules containing poloxalkol 0.25 Gm. and casanthranol 30 mg.; syrup containing in each 5 ml. poloxalkol 0.25 Gm. and casanthranol 30 mg.
PACKAGING: Capsules, bottles of 16 and 100 capsules; syrup, bottles of 4 and 16 ounces.
SUPPLIER: Upjohn Co.

Feosol Spansules

GENERIC NAME: Ferrous sulfate.
INDICATIONS: Simple iron deficiency anemias; avoids usual side effects of iron therapy with use of sustained release capsules.
DOSAGE: One capsule daily for mild iron deficiency anemias; one capsule twice daily for more severe iron deficiency anemias or where more rapid hemoglobin regeneration is necessary.
PREPARATIONS: Capsules containing 150 mg. exsiccated ferrous sulfate, equivalent to 225 mg. Ferrous Sulfate U.S.P.
PACKAGING: Bottles of 30 capsules.
SUPPLIER: Smith, Kline & French Laboratories.

Hydropres

COMPOSITION: . Hydrochlorothiazide with reserpine.
INDICATIONS: Hypertension, providing smooth maintenance of blood pressure within normo-tensive limits.
SIDE EFFECTS AND CONTRAINDICATIONS: As with other diuretics, patient must be carefully watched for early signs of fluid and electrolyte imbalance; caution is indicated in renal and hepatic edema and in patients with advanced cirrhosis and hepatic disease.
DOSAGE: Varies from one tablet daily to one tablet Hydropres-25 four times daily or one tablet Hydropres-50 twice daily.
PREPARATIONS: Tablets cotaining hydrochlorothiazide 25 or 50 mg. with reserpine 0.125 mg.
PACKAGING: Hydropres-25 and Hydropres-50, bottles of 100 and 1,000 tablets.
SUPPLIER: Merck Sharp & Dohme.

Lidosporin Otic Solution

COMPOSITION: Polymyxin (Aerosporin) B sulfate, lidocaine (Xylocaine) hydrochloride, in propylene glycol.
INDICATIONS: For treatment of infection, pain and itching associated with otitis externa, otitis media (if tympanic membrane is perforated), otomycosis, postoperative aural cavities, and furunculosis.
DOSAGES: After preliminary cleansing and drying, 3 or 4 drops are instilled into infected ear, 3 or 4 times daily. Solution may be applied by saturating a gauze or cotton wick, which may be left in canal for 24 to 48 hours, keeping wick moist.
PREPARATIONS: Solution containing in each ml. polymyxin B sulfate 10,000 units and lidocaine hydrochloride 50 mg., in propylene glycol.
PACKAGING: Bottles of 10 ml. with dropper.
SUPPLIER: Burroughs Wellcome & Co.

Marax

COMPOSITION: Hydroxyzine (Atarax) hydrochloride, ephedrine sulfate, and theophylline.
INDICATIONS: To control bronchospastic disorders and allied conditions.
SIDE EFFECTS AND CONTRAINDICATIONS: Contraindicated in cardiovascular disease, hyperthyroidism, and circulatory disease.
DOSAGE: One tablet 2 to 4 times daily; children, over 5 years of age, one-half the adult dose.
PREPARATIONS: Tablets containing hydroxyzine hydrochloride 10 mg., ephedrine sulfate 25 mg., and theophylline 130 mg.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Roerig.

Mellaril

GENERIC AND CHEMICAL NAMES: Thioridazine hydrochloride; 2-methylmercapto-10-[2-(N-methyl-2-piperidyl) ethyl]-phenothiazine hydrochloride.
INDICATIONS: Ataractic drug.
DOSAGE: As directed by physician.
PREPARATIONS: Tablets of 10 mg., 25 mg., and 100 mg.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Sandoz.

Mornidine

GENERIC NAME: Pipamazine; 10-[3-(4-carbamoylpiperidino)-propyl]-2-chlorphenothiazine.
INDICATIONS: Antinauseant and antiemetic for nausea or vomiting associated with pregnancy, anesthesia, radiation therapy, nitrogen mustard therapy and gastroenteritis.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasional drowsiness.

DOSAGE: Adults, 5 mg. orally or parenterally every 4 to 6 hours as needed. Usual parenteral route is intramuscular but if intravenous injection is necessary, it should be given slowly over a period of 5 minutes.
PREPARATIONS: Ampuls 5 mg. per ml., 1 ml., containing 2 mg. ascorbic acid and 2 mg. sodium bisulfite in aqueous solution; tablets of 5 mg.
PACKAGING: Ampuls, boxes of 6 and 25 ampuls; bottles of 100 and 500 tablets.
SUPPLIER: G. D. Searle & Co.

Nardil

GENERIC NAME: Phenelzine dihydrogen sulfate.
INDICATIONS: Antidepressant in true depression (endogenous, essential, primary, non-reactive) of either the larval or overt type; improves depressed phase of affective (manic-depressive) psychoses; of value in relieving depression of catatonic schizophrenics, although not affecting the psychosis *per se*.
SIDE EFFECTS AND CONTRAINDICATIONS: Include postural hypotension, transient impotence, nausea, ankle edema, delayed micturition, and constipation.
DOSAGE: Initially, 15 mg. three times daily; maintenance level may be as low as 15 mg. daily or every other day.
PREPARATIONS: Tablets, 15 mg., coated.
PACKAGING: Bottles of 100 tablets.
SUPPLIER: Warner-Chilcott.

Ophthocort

COMPOSITION: Chloramphenicol (Chloromycetin), hydrocortisone acetate, and polymyxin B sulfate.
INDICATIONS: For viral inflammation and nonviral iridocyclitis, with or without ulcer, involving the eye and adnexa; provides antibacterial, anti-inflammatory and antiallergic action in ocular inflammations complicated by infection.
SIDE EFFECTS AND CONTRAINDICATIONS: Should not be used in patients with ocular tuberculosis or herpes simplex.
DOSAGE: First 24 to 48 hours, applied to affected eye 2 to 4 times daily; after 24 to 48 hours, continued until eye appears normal for 48 hours.
PREPARATIONS: Ophthalmic ointment containing 1 percent chloramphenicol, 0.5 percent hydrocortisone acetate, and 5,000 units polymyxin B sulfate per Gm.
PACKAGING: Tubes of ⅛ ounce.
SUPPLIER: Parke, Davis.

Rezifilm

COMPOSITION: A methacrylate resin with tetramethylthiuram disulfide dissolved in ethyl acetate, with dichlorodifluoro- and tri-chloromonofluoromethane as the propellents.
INDICATIONS: Preoperatively and postoperatively to protect operative site; protects from exogenous microorganisms, lets the skin "breathe," permits evaporation of perspiration and penetration of air, need not be removed at time of operation—incision can be made through film.
SIDE EFFECTS AND PRECAUTIONS: When used on the face, care should be taken to avoid the eyes and to prevent inhalation. Do not puncture or incinerate can. Keep away from open flame.
DOSAGE: Applied to a dry surface. Holding can 6 to 8 inches away from area, apply enough to cover the affected surface and adjacent area with a continuous firm film. Acetone may be used for removing the film.
PREPARATIONS: A methacrylate resin containing 0.6 percent tetramethylthiuram disulfide.
PACKAGING: Aerosol dispenser cans of 2 ounces.
SUPPLIER: Squibb.

THIO-TEPA

CHEMICAL NAME: N,N′,N″-triethylenethiophosphoramide, a polyfunctioning alkylating agent related chemically and pharmacologically to nitrogen mustard.
INDICATIONS: In the palliation of a large variety of neoplastic disease; more consistent results have been seen in adenocarcinoma of the breast and ovary, lymphoma and melanotic sarcoma.
SIDE EFFECTS AND CONTRAINDICATIONS: THIO-TEPA is a drug of high toxicity for the hematopoietic system; a rapidly falling white blood or platelet count indicates the necessity for discontinuing or reducing the dosage of the drug. For additional precautions, see package literature.
DOSAGE: Has been administered by the following routes: oral, intravenous, intra-arterial, intramuscular, intratumor, and intraserosal. See literature for detailed dosage.
PREPARATIONS: Vials containing 15 mg. for parenteral use.
SUPPLIER: Lederle Laboratories.

Triburon Vaginal Cream

COMPOSITION: Triclobisonium (Triburon) chloride 0.1 percent, in a white hydrophilic cream.
INDICATIONS: Microbicidal for control of vaginitis and vulvitis due to *Trichomonas vaginalis, Candida ablicans* and *Hemophilus vaginalis,* as well as for those infections in which staphylococci and streptococci are the causative organisms.
DOSAGE: One applicatorful should be introduced into the vagina every night for two weeks; safe to use during pregnancy, and therapy need not be interrupted during menstruation.
PREPARATIONS: Cream containing 0.1 percent triclobisonium chloride.
PACKAGING: Vaginal cream, packaged with 18 disposable applicators.
SUPPLIER: Roche Laboratories.

Vasodilan

GENERIC AND CHEMICAL NAMES: Isoxsuprine hydrochloride; 1-(*p*-hydroxyphenyl)-2-1′-methyl-2′-phenoxyethylamino)-propanol-1 hydrochloride.
INDICATIONS: For symptomatic relief of painful menstrual cramps due to uterine muscle spasm, and for threatened abortion or premature labor where uterine relaxation may be of value.
SIDE EFFECTS AND CONTRAINDICATIONS: Occasional palpitation and dizziness; intramuscular injection is not recommended in presence of tachycardia or hypotension. Intravenous administration is not recommended.
DOSAGE: For dysmenorrhea, 10 to 20 mg. orally 3 or 4 times daily 24 to 72 hours prior to expected onset of menstruation; 5 to 10 mg. may be given intramuscularly in severe, intractable dysmenorrhea, followed by oral maintenance. For threatened abortion or premature labor, 10 mg. is administered intramuscularly, followed by a second injection within 4 hours if indicated.
PREPARATIONS: Injection, 5 mg. per ml., 2 ml. ampuls; tablets, 10 mg.
PACKAGING: Injection, boxes of 6 ampuls; tablets, bottles of 100 tablets.
SUPPLIER: Mead Johnson.

Consulting WITH BOWLES

GROVER C. BOWLES JR., *Baptist Memorial Hospital, Memphis, Tennessee*

► To whom do you surrender damaged, contaminated or out-dated narcotic drugs?

Unusable narcotics may be surrendered to the District Supervisor of your narcotic district. The usual procedure is to request permission by writing to the District Supervisor. He will send you four copies of Form 142 which should be completed, properly signed and included with the narcotics surrendered. Surrendered narcotics should be shipped or expressed prepaid (not mailed) to the Office of the District Supervisor. One copy of Form 142 will be returned to you and should be filed with your narcotic records.

Some companies will permit the return of unopened packages of narcotics when the tax stamp is still intact for credit. Permission should be first obtained from the District Director of Internal Revenue. Once this permission has been obtained and an official narcotic order form has been received from the supplier, the narcotic specified on the order may be returned (shipped or expressed not mailed) for credit. The narcotic order form is then filed with your other narcotic records.

► Where can we find information about the active ingredients found in the commonly used pesticides?

The *Pesticide Handbook*, edited by Donald E. H. Frear, Ph.D., professor of agricultural and biological chemistry, The Pennsylvania State University is an excellent source of information about the content of pesticides. The active ingredients of some 7041 insecticides, fungicides, herbicides, rodenticides and soil conditioners are listed in the 11th. edition recently published.

The *Pesticide Handbook* is revised each year and is available from the College Science Publishers, State College, Pennsylvania. The paper edition is $1.75 and the cloth bound edition is $3.25.

Clinical Memoranda on Economic Posions available from the Superintendent of Documents, U. S. Government Printing Office, Washington 52, D. C. is another publication dealing with the toxicity of pesticides which hospital pharmacists will find of value. The cost of this publication is $ .30 and it is designated as Public Health Publication No. 476.

► What is Actamer and who makes it?

Actamer is Monsanto's registered trade mark for Bithionol, U.S.P. Chemically, this compound is 2, 2' thiobis(4,6 dichlorophenol). Classified as a local anti-infective agent by the U.S.P., bithionol is added to toilet soaps, shampoos, cosmetics, etc. to inhibit the growth and reproduction of susceptible skin bacteria. It is said to be effective against many common skin bacteria and some pathogenic fungi at concentrations of 10 parts per million. Concentrations of 3 to 5 percent are recommended for surgical scrub soaps.

Additional information is available from the Monsanto Chemical Company, Organic Chemicals Division, Lindbergh & Olive Street Road, St. Louis 24, Missouri. Of interest also, will be the article, "Comparisons Between Phisohex, Actamer and Septisol as Germicidal Agents for the Skin" by Hopper, Beck and Wood, published in *The Bulletin of the American Society of Hospital Pharmacists, May-June 1953.*

► Please differentiate between chelating agents, sequestering agents and complexing agents.

Chelating agents are compounds that will inactivate a metallic ion by making the metallic ion an integral part of an inner ring structure.

Sequestering agents are compounds that will inactivate a metallic ion by forming a water-soluble complex in which the metal is held in a non-ionizable form.

Complexing agents are compounds that will inactivate a metallic ion.

► Should the pharmacy inventory be taken by a paid inventory group or by the pharmacy personnel?

Unless the hospital administration insists that the inventory be taken by an outside group, I feel that it should be taken by the pharmacy staff.

The usual fee charged by outside inventory groups is usually from 1 to 2 percent. Thus cost is no small item. More important, inventory time provides an excellent opportunity for the pharmacy staff to systematically eliminate obsolete, unusable and hazardous items from the inventory. Taking inventory is still the best method for the pharmacy staff to become acquainted with the stock and the location of infrequently used items.

► What arrangements can be made in a one-pharmacist operation for vacation relief?

Frequently, arrangements can be made with a local pharmacist to spend at least part of each day in the pharmacy. Usually, wholesale drug firms can assist you if help is needed in locating a relief pharmacist. In some areas of the country, relief pharmacists ride circuit and arrangements can be made with them, usually several months in advance, for coverage while you are away. Ideally, of course, you would have a registered pharmacist on duty in your place during the normal hours the pharmacy is open so no interruption of pharmacy service would result while you are on vacation.

News

A.H.A. Annual Meeting

The American Hospital Association is holding its sixty-first Annual Meeting in New York City, August 24-27. Highlights of the Convention include Leona Baumgartner, M.D., who will be the Auxiliaries Luncheon Speaker on Monday; His Eminence Francis Cardinal Spellman, Archbishop of New York, who will speak at the Catholic Sisters Luncheon on Monday; and General Alfred N. Gruenther, President of the American National Red Cross, who will be the speaker at the Federal Hospital Executives Luncheon on Tuesday. Other speakers during the week include Francis Boyer, Chairman of the Board, Smith Kline & French Laboratories; Francis J. Braceland, M.D., Psychiatrist-in-Chief, The Institute of Living, Hartford, Connecticut; Dr. M. G. Candau, Director General, World Health Organization; and Elmo Roper and Associates, New York City.

Other items of interest at the A.H.A. Convention include the Architectural Exhibit, the Film Exhibit, and the Hospital Merchandise Mart. The Architectural Exhibit will show new developments in hospital architecture. The Film Exhibit will present two films daily, 12:00-1:15. Included are: "Explosion Hazards from Flammable Anesthetics," "A New World for Peter," "No Margin for Error," "A Place for Healing," "Healthward Ho!" "Helping Hands for Julie," "Hospital Sepsis: A Communicable Disease." The Hospital Merchandise Mart brings together under one roof the world's largest display of hospital supplies, equipment and services.

Meetings and exhibits will be held at the New York Coliseum with the Statler-Hilton as the Headquarters Hotel.

► Alfred A. Mannino, Executive Director, Hospital Department, McKesson & Robbins, Inc., spoke recently before the Southern California Society of Hospital Pharmacists at the University of California Conference Center, Lake Arrowhead, California.

Mr. Mannino's subject "Pharmacy Purchasing and Inventory Control" covered various methods of purchasing, sources of supply, essential records and factors in inventory control.

► Dr. William H. Kessenich has recently been appointed Medical Director of the Food and Drug Administration. This has been announced by George P. Larrick, Commissioner of Food and Drugs.

Dr. Kessenich has been Acting Medical Director since January 17 of this year, and will direct the staff of physicians and veterinary medical officers in the FDA's Bureau of Medicine. He will advise the Commissioner of Food and Drugs, with respect to the agency's policy, on the effectiveness and safety of drugs, devices, and cosmetics. He will also direct clinical studies, review new drug applications, and serve as expert consultant to the government in court cases involving medical testimony.

► Cedric Jeffers, Chief Pharmacist at Scott and White Hospital, Temple, Texas, and Robert Lantos, Director of Pharmacy Service, The University of Texas —Medical Branch, Galveston, participated in a panel on "The Interprofessional Relationships of Retail and Hospital Pharmacy," at the Annual Convention of the Texas Pharmaceutical Association. The meeting was held in Fort Worth on July 27.

► Robert Lantos, Director of Pharmacy Service at The University of Texas—Medical Branch, Galveston, participated in a Pre-Pharmacy Advisor's Conference in Austin on July 6. Sponsored by the College of Pharmacy Extension Service of The University of Texas, the Conference was attended by deans and student counselors of junior colleges and small senior colleges of the State. Representatives of the different phases of pharmacy spoke to the counselors so that they may in turn advise their students in selecting a pre-pharmacy course. Mr. Lantos spoke on the opportunities in hospital pharmacy.

A.I.H.P. Awards Urdang Medal To French Pharmacist-Historian

The American Institute of the History of Pharmacy announces that the fifth Urdang Medal has been conferred upon Maurice Bouvet, pharmacist-historian of Paris.

The Medal honors unusually distinguished historical publications on pharmacy appearing anywhere in the world. A special committee of the International Academy of the History of Pharmacy aids in selecting recipients. The first Urdang Medal was struck on the seventieth birthday (1952) of the former Director of The American Institute of the History of Pharmacy, who himself did so much to further a historical literature of pharmacy and high standards of historical writing.

In recommending the 74-year-old Parisian as the fifth Medalist, the Committee selected a man of Urdang's own generation as well as standard of scholarship. Dr. Bouvet was cited particularly for his definitive book on the development of pharmacy in France

(*Histoire de la Pharmacie en France des Origines à Nos Jours,* Paris, 1936, 445 pp.), as well as his monographic research on such topics as the French health professions during the American Revolution and the history of pharmacy (*Le Service de Santé Francais pendant la Guerre d'Indêpendance des Etats-Unis (1777-1782)*, Paris, 1934, 111 pp., and *La Pharmacie Hospitaliére à Paris de (1789 à 1815,* Paris, 1934, 92pp.).

For his distinguished writings, Dr. Bouvet received the Medal from the hand of Professor Alex Berman of the University of Michigan, a Councillor of the American Institute of the History of Pharmacy who is now in Europe as a Guggenheim Fellow. The ceremony was held at a meeting of the French Society for the History of Pharmacy convened at the School of Pharmacy of Paris in the "Salle des Actes," which has been referred to as "probably the most elegant room in any school of pharmacy."

In presenting the Medal, Professor Berman praised Dr. Bouvet as "a prolific author held in world-wide esteem. Any scholar who wishes to study and describe the development of pharmacy in France," he concluded, "must take into account the numerous monographs written by M. Bouvet, which constitute a veritable treasure house."

Other recipients of the Medal during the seven years since its establishment have been Josef A. Häfliger of Switzerland; Eugéne-Humbert Guitard of France; Rafael Folch Andreu of Spain; and D. A. Wittop-Koning of The Netherlands.

Colonel Roy D. Maxwell Appointed Chief of Army Medical Service Corps

Colonel Roy D. Maxwell, one of the foremost authorities on nuclear radiation and radiation fall-out, has been named Chief of the Army's Medical Service Corps effective 1 July 1959 the Army Surgeon General's Office announced today. Since January 1957 Colonel Maxwell has been Assistant for Nuclear Warfare Instruction and Casualty Studies, Army Medical Service School at Brooke Army Medical Center, Fort Sam Houston, Texas.

As chief of the Medical Service Corps, one of the six Corps that comprise the U. S. Army Medical Service, Colonel Maxwell will head the Corps charged with providing the scientific, technical, and administrative services to the U. S. Army Medical Service in the care of the sick and wounded, and in maintaining the health of the Army.

In 1946 Colonel Maxwell served as Radiological Safety Officer in the Atomic Bomb tests at Bikini. Since that time he has attended many tests of nuclear and thermonuclear weapons in the Pacific area and at the New Mexico proving grounds. Prior to assignment at Brooke, he was Chief of the Fall-out Group in the Armed Forces Special Weapons project at Sandia Base, New Mexico.

Besides his work with atomic weapons effects, Colonel Maxwell is well known as a biochemist. He was Chief of the Department of Biophysics at the Army Medical Service Graduate School in Washington, D.C., from 1949 to 1951 and Director of the Physiology and Pharmacology Division at the School until 1955.

Colonel Maxwell took an A.B. degree in chemistry at Oklahoma City University, and subsequently earned his M.S. and Ph.D. degrees at the University of Iowa in organic chemistry. Following his work at the Bikini tests "Operation Crossroads," he did postgraduate study in radiochemistry and biophysics at the University of California for two years. He is also a graduate of the Army's Command and General Staff College at Fort Leavenworth, Kansas.

The Colonel is a member of the American Chemical Society, and Alpha Chi Sigma Chemistry Fraternity. He is co-author of several published reports and articles, as well as serving as a consultant for the Army in problems incident to radioactive fall-out.

Colonel Maxwell succeeds Colonel Bernard Aabel who has completed his tour of duty as Chief of the Medical Service Corps.

V. A. Pharmacy Resident Awarded Certificate

Mr. Norman S. Hammelman, Chief, Pharmacy Service, has recently announced that Mr. Kurt Kleinmann has completed the joint program of graduate study at the St. Louis College of Pharmacy, receiving a Master of Science Degree and completing the Residency in Hospital Pharmacy affered by the Veterans Administration Hospital in St. Louis. On completion of the program, Dr. John W. Claiborne, Manager of the V.A. Hospital, presented the Certificate of Internship to Mr. Kleinmann.

Shown left to rights John W. Claiborne, M.D., Manager, Veterans Administration Hospital, St. Louis; Kurt Kleinmann, Pharmacy Resident; and Norman Hammelman, Chief, Pharmacy Service

as the president sees it—

VERNON O. TRYGSTAD, *Veterans Administration, Washington, D. C.*

► AS YOUR NEW PRESIDENT, I am looking forward to discussing with you throughout the year some of the goals and problems of our vigorous, young specialty. From time to time this page will be taken over by Vice President Jack Heard, whose views and comment I know will be interesting and stimulating.

I have just taken a closer look at the objectives of the SOCIETY as defined in the Constitution. I recommend this closer look to all of our members. Predominant is emphasis on the skill, qualifications, and education of hospital pharmacists; and on our responsibility to provide for an adequate supply of qualified hospital pharmacists.

We must encourage students and graduate pharmacists, whose interests lie in hospital pharmacy, to concentrate their early training and experience in this field. We must ensure that there are ample opportunities for orientation, training, and practical experience in hospital pharmacy. Finally, the practical experience thus gained must be legally recognized on an equal basis with practical experience acquired in retail pharmacy.

Nearly ten percent of all pharmacy graduates today go into hospital pharmacy. Some do so with little or no prior experience in a hospital, the required practical experience being limited to retail pharmacy. The needs of hospitals and of future hospital pharmacists would be better served if the required internship—the legally required period of "practical experience"— of those pharmacists who choose hospital service, could be spent in a hospital pharmacy.

In a majority of States, hospital pharmacy experience fully meets the practical experience requirement for registration. But in five States, no credit is given for hospital experience; and in nine more, hospital pharmacy experience is credited for only half the requirement. In these cases, the remainder must be in retail pharmacy. Is this any longer a logical or necessary requirement?

I do not know the reason for the variations in State laws. I believe we should find out what those reasons are. Could it be that these restrictive State requirements have not been revised since hospital pharmacy emerged as a specialty? And that the need for and quality of hospital pharmacy experience has changed since those laws and regulations were put into effect? Or could it be that we have failed to point out the thoroughness, the professional advantages, the desirability of hospital pharmacy experience? I wonder if we should not examine ourselves first. Have we as hospital pharmacists failed to communicate effectively with Boards of Pharmacy, to point out the advantages of preparation for a pharmacy career through hospital training, and the real quality of professional experience to be gained in hospitals? Have we told the story of hospital pharmacy, and told it effectively? How many State Board members do *you* know, and how many have seen *your* pharmacy in operation? How many have been guests at your local Chapter or State Society meetings?

Our need to gain State Board acceptance for hospital pharmacy experience, universally, is clear. Then, we must ensure that opportunities really exist for all who seek specialized training and experience in our field. On-the-job training positions must be available, and pharmacy students and graduates must be encouraged to take them. I am not advocating practical experience in all cases as a substitute for formal residencies or internships combined with graduate degree programs. These are most desirable and necessary for providing a source of specialized, highly skilled, key pharmacists. But production of graduate degree hospital pharmacists is not keeping up with total manpower needs. With longer academic courses, it may be that fewer registered pharmacists will be able to spend additional time in postgraduate residencies. Many of our successful future hospital pharmacists, as in the past, will rise through the ranks. It is important to recognize, then, that a year in a good hospital pharmacy will make a better prepared pharmacist for hospital service than a year in a drugstore. In the Minimum Standards for Internships in Hospital Pharmacy, we have the advantage of guidelines which can assure a well-rounded indoctrination into the major aspects of hospital pharmacy practice. Thus applied, the quality of hospital experience can meet the most rigid comparison with other types of pharmacy "practical experience" or internship.

Providing the opportunities for good, sound hospital pharmacy experience, and assuring recognition of this experience by State Boards of Pharmacy will increase the supply of pharmacists for professional work in our hospitals. Let's work toward this goal.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

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edited by CLIFTON J. LATIOLAIS, HENRY J. DEREWICZ *and* LEO F. GODLEY

CORING OF RUBBER CLOSURES

Factors Influencing the Coring of Rubber Closures, Hopkins, G. H., Bull. Parenteral Drug Assoc. 13:17 (Jan.-Feb.) (1959). The West Company, Phoenixville, Pa.

Coring of rubber closures in multiple dose vials is the result of gouging by the sharp heel of a hypodermic needle against the relatively rigid diaphragm. To evaluate the factors influencing the coring rate, the rubber and elastomer formulations, diaphragm design, sealing procedure, closure preparation and treatment, and the needle design were considered in the investigation.

In summary, three factors contributed most to the reductions of cores, that is (1) the use of a needle with a dull heel, (2) a diaphragm design utilizing a reverse sealing head pressure block, and (3) formulations with the least possible inorganic reinforcement. Other factors include the use of the lowest effective head pressure in sealing, processing closures with the least possible heat exposure, use of closures with the lowest coring, modification of closure formulations with silicone or paraffin wax, the use of closures with a concave top surface and also plug-type stoppers in place of flat discs, and a thinner diaphragm to be punctured.

NORMAN HO

TETRACYCLINE AND CHLORTETRACYCLINE ASSAY

The Spectrophotometric Assay for Chlortetracycline Hydrochloride and Tetracycline Hydrochloride in Pharmaceuticals, Chiccarelli, F., Woolford, M., and Avery, M., J. Am. Pharm. Assoc., Sci. Ed. 48:263 (May) 1959. (Lederle Laboratories Division, American Cyanamid Company, Pearl River, N.Y.)

Specific spectrophotometric assays have been developed for tetracycline hydrochloride and chlortetracycline hydrochloride. Essentially the assay is based upon the formation of anhydrotetracyline and anhydrochlortetracycline when both compounds are heated under acid conditions. Since both anhydrotetracycline and anhydrochlortetracycline have similar spectrophotometric properties, a distinction is unreliable. However, specified assays have been developed for the anhydro compounds in addition to the fact that chlortetracycline heated at pH 7.5 is cleaved to isochlortetracycline while tetracycline under the same conditions is relatively stable. Detailed methods are described for adapting the assay for use with all of the various dosage forms containing both tetracycline hydrochloride and chlortetracycline hydrochloride.

HENRY J. DEREWICZ

PENICILLIN, ABSORPTION DIFFERENCES IN ORAL

Individual Differences in the Absorption of Peroral Penicillin, Lange. Von Adalbert and Volkening, R., Arzneimittel Forschung, 9:64 (Jan.) 1959.

Maximal penicillin concentration in the serum at individually different times following peroral application of a penicillin preparation is demonstrated. Maximal concentrations were observed early in one group of persons (after 1 hr.), after a medium interval in a second group (2 hrs.), and late (after 4 hrs.) in a further group. Eight of the 23 test persons, who received 100,000 units phenoxymethyl penicillin, belonged to the group with an early maximal concentration, 10 to the group with a medium interval and 5 to the late group. After increase of the penicillin dose to 200,000 units, the distribution among 16 test persons was as follows: early maximal concentration in 11, after medium interval in 3 and late in 2 persons. In experiments with potassium phenoxymethyl penicillin 13 persons out of 15 belonged to the group with an early maximal concentration, 2 to the medium group, following application of 100,000 units. After oral application of 200,000 units, only the group with early maximal concentration was to be found in all 15 individuals. Following application of a combination of 100,000 units of potassium phenoxymethyl penicillin and phenoxymethyl penicillin each, 14 out of 18 test persons belonged to the group with an early maximal concentration, 2 to the one with a medium interval and 2 to the late group.

The observation of maximal penicillin concentrations in the serum at individually different times stresses the necessity to compare only such blood levels as show the maximal concentration at the same time. Accordingly test persons will have to be divided into groups subjected to separate observation owing to different reaction. In a comparison of the investigated perorally applied penicillin preparations along these lines, potassium phenoxymethyl penicillin proved superior to phenoxymethyl penicillin in regard to attainable maximal concentrations. It has been possible to show, that 1, 2 and 4 hrs. after oral application of a combination of 100,000 units potassium phenoxymethyl penicillin and phenoxymethyl penicillin each, higher penicillin concentrations in the serum are found than following 200,000 units each of the components of the combination.

The differences of maximal concentrations in the serum at different times in human beings are interpreted as the result of individually different absorption of penicillin preparations. These individual differences of absorption are observed more clearly in sparingly soluble penicillin preparations, as for instance in phenoxymethyl penicillin as an acid than in the early soluble potassium salt of phenoxymethyl penicillin.

AUTHOR'S SUMMARY

TESTOSTERONE PROPIONATE INJECTION, STABILITY OF

The Stability of Injection of Testosterone Propionate 5% Pedersen, Vagn Jorgen, Dansk Tidssk. Farm., 33:17 (Feb.) 1959.

Several authors have published methods for the determination of testosterone, testosterone propionate and other ketosteroids. Diding has developed a method for the determination of testosterone propionate dissolved in peanut oil. This method was based on a distribution extraction (15 extractions) of testosterone, precipitation of the steroid with dinitrophenylhydrazine for 6 hours and a spectrophotometric determination at 390 M_μ of the dinitrophenylhydrazine dissolved in chloroform.

This method has been further developed by Pedersen who found that Injection of Testosterone Propionate 5% can be assayed without any isolation of testosterone propionate. The dinitrophenylhydrazine has in this case to be in contact with the injection solution for 24 hours just as the value of the blank determined on the solvent has to be subtracted.

One preparation of Injection of Testosterone Propionate 5% was made up and distributed in 1 ml. ampuls and 10 ml. vials. A third of the vials received no heat treatment, whereas the other two parts were treated at 140° C. for 3 hours and at 160° C. for 2 hours, respectively. The authors give the analytical results obtained on injection solutions stored 1½, 4, 9, 18, and 24 months at room temperature. The assay of 3 older injection solutions is given. With the analytical method used, the results obtained seem to indicate that Injection of Testosterone Propionate can be stored several years. As a supplement of earlier published communications on the analytical method, the influence of the time of precipitation was investigated and the results are given. Quantitative precipitation of the dinitrophenylhydrazine was accomplished in 18 hours, but due to practical reasons, 24 hours of precipitation was chosen.

Testosterone propionate dissolved in absolute ethanol (originally used for the standard curve) was analyzed

and after 10 months the values were 1% too high compared with the standard curve. After 18 months the values were 3% too high.

AUTHOR'S SUMMARY

ANTIBACTERIAL ACTIVITY OF VOLATILE SUBSTANCES

Studies on Antibacterial Vapors of Volatile Substances, Grubb, T. C., J. Am. Pharm. Assoc., Sci. Ed. 48:272 (May) 1959. (Vick Chemical Company, Bloomfield, N.J.)

Two simple methods are described for making quantitative estimates of both bacteriostatic and bactericidal activities of vapors from volatile compounds which might be used therapeutically rather than those compounds which are used on inanimate objects. Such compounds as thymol, menthol, chlorthymol and turpentine oil were evaluated using *S. aureus* and *Klebsiella pneumoniae*. One method is used for static exposure periods of twelve to eighteen hours, the other is for dynamic exposure periods as short as one second. Results against the types of bacteria commonly associated with respiratory infection indicate that many of the drugs which have been employed empirically many years for inhalation therapy of respiratory infections, display a measurable degree of *in vitro* antibacterial and antiviral activity.

HENRY J. DEREWICZ

MICROESTIMATION OF OPIUM ALKALOIDS

Microestimation of Opium Alkaloids in Pharmaceuticals by Paper Chromatography, Genest, K. and Farmilo C., J. Am. Pharm. Assoc., Sci. Ed. 48:286 (May) 1959. (The Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Canada.)

A method of analysis for morphine, codeine, thebaine, and papaverine in micro quantities in pharmaceutical preparations is described. The process which employs paper chromatography for separation followed by densitometric evaluation with a self-integrating densitometer enables the quantation to be achieved more rapidly than by usual procedures involving elution, photographic reproduction or manual planimetry. The procedure is applicable to a wide range of alkaloids and synthetic basic compounds. Application of the method is made to the assay of small samples of narcotics received in legal cases and to the analysis of opium for purposes of determination of country of origin.

HENRY J. DEREWICZ

AIR HYGIENE FOR HOSPITALS

Air Hygiene for Hospitals: II. Efficiency of Fibrous Filters Against Staphylococcic Droplet Nuclei and Bacteria-Bearing Dust, Allen, H. F., J. Am. Med. Assoc. 170:261 (May 16) 1959. (Bacteriology Laboratory, Massachusetts Eye and Ear Infirmary, and Department of Ophthalmology, Harvard Medical School)

This study reports the efficiency of fibrous filters against airbone bacteria-bearing particles in experimental and actual conditions. In the preliminary report, four types of filtering devices are briefly discussed, that is, filters coated with viscous materials, dry porous mediums, electrostatic precipitation filters, and filters of wet pores or fine sprays. Only the dry porous filters are considered in the study. Such filters of glass fibers average between 0.8 and 3.0 microns in diameter and are rated by National Bureau of Standards' tests in terms of their efficiency against atmospheric dust and dioctyl phthalate smoke. Bacteria in air occurring as droplet nuclei or adhering to dust particles range between 1.34 and 2.68 microns in diameter.

A filter blower system was adapted for bacterial sampling of staphylococcic droplet nuclei and bacteria-bearing dust particles. Sampling rates were 2.0 to 4.0 liters per minute. Air filters (CM 114, Micretain, Fiberfax, Filterdown 50-FG, Aerosolve 95, and Aerosolve 85) were tested. Retention of droplet nuclei ranged from 89 to 99.97 percent and of dust-borne bacteria over 99 percent. Their efficiency increased with the useful life of the filter as the particles accumulate.

In the survey utilizing the ventilating system to two operating room suites, the efficiency of the filters to nebulized staphylococci was reported in the order of 95 percent. The air flow was between 500 and 600 cubic feet per minute.

This study pointed out the possibility of providing highly efficient filteration of dust-borne bacteria and bacterial droplet nuclei through the installation of certain deep-bedded glass fiber filtering medium in the hospital ventilating system to operating rooms, delivery rooms, and nurseries. The filter pads are economical (service life of approximately 4,000 hours), highly efficient, and uniform.

NORMAN HO

MICRO-FILTRATION IN PRODUCTION OF PARENTERALS

Micro-Filtration in the Production of Parenterals, Jordan, George V., Bull. Parenteral Drug Assoc. 13:21 (Jan.-Feb.) 1959. (Selas Corporation of America, Dresher, Pa.)

Microfiltration consists of three phases, namely clarification, polishing, and cold sterilization, each defined according to the range of particle sizes retained by a micro-porous membrane. The grades of microfilters depend upon the openings per square inch or the size of the radius per opening, measured in micros. Cold sterilization may be defined as the removal of all pathogenic organisms and particles down to approximately 0.3 micron by a micro-porous membrane having 1.5 billion openings per square inch—none of which is greater than 0.6 microns in radius. The filtration is accomplished by a combination of three phenomena: adsorption, particle retention, and electric charge.

NORMAN HO

EMULSIFYING AGENTS IN SUPPOSITORY BASES

A Study of the Effect of Some Emulsifying Agents on Drug Release from Suppository Bases, Whitworth, C. and Larocca, J. P., J. Am. Pharm. Assoc., Sci. Ed. 48:353 (June) 1959. (University of Georgia, School of Pharmacy, Athens, Ga.)

A study of suppository bases consisting of hydrogenated cottonseed oil, in varying amounts, combined with different synthetic emulsifying agents was conducted in search of better water-miscible bases. The percent drug released, the stability, and the melting range of the various bases compounded were ascertained. Using a few of the bases under study, an *in vivo* comparison of the rectal absorption was made with a commercial brand suppository. Results proved the bases containing Tween products to be the most effective in drug release. However, this was attributed to the use of a water-soluble drug. The authors found that good release of the drug could be obtained through the use of a base made from hydrogenated cottonseed oil, containing 35-40% of the emulsifying agents, and having a melting range of less than 48°C. They reported all suppositories were quickly and easily compounded yielding a smooth and pleasing final appearance.

H. A. K. WHITNEY, JR.

BINDING OF SURFACTANTS

Interaction of Preservatives With Macromolecules II, Pisano, F. D. and Kostenbauder, H. B., J. Am. Pharm. Assoc., Sci. Ed., 48:310 (June) 1959. (School of Pharmacy, Temple University, Philadelphia, Pa.)

Experiments were conducted to show the effect of nonionic surfactants on the ability of parahydroxybenzoates (parabens) to inhibit bacterial growth. Numerous problems which could interfere with the results are discussed and solved. The percentages of paraben necessary to inhibit growth in different concentrations of surfactant were determined. The amount of bacterial growth, at varying concentrations of paraben, in a medium without surfactant is compared to a medium containing a surfactant. It is shown that the parabens are bound to nonionic surfactants in aqueous solutions, and that, in these solutions, bacterial inhibition is dependent on the percent of free paraben available. A method is devised to determine the concentrations to be used when a preservative is employed in a solution containing a surfactant. The binding power of different esters of p-hydroxybenzoic acid with several of the polyoxyethylene surfactants is reviewed. Methylparaben in aqueous solutions was found to be a better preservative when a nonionic surfactant was present. However, in the absence of a surfactant, the propyl and butyl esters were more effective.

H. A. K. WHITNEY, JR.

BINDING OF SURFACANTS

Interaction of Preservatives With Macromolecules III, Miyawaki, G. M., Patel, N. K., and Kostenbauder, H. B., J. Am. Pharm. Assoc., Sci. Ed., 48:315 (June) 1959. (School of Pharmacy, Temple University, Philadelphia, Pa.)

This is the third article in a series of studies concerned with the effects of macromolecules on the p-hydroxy-

benzoates (parabens). The macromolecules in this investigation were: tragacanth, gelatin, carboxymethylcellulose (CMC), polyethylene glycol (PEG) 4000, methylcellulose, and polyvinylpyrrolidone (PVP). Many of the testing procedures used were identical to those carried out in the first two reports. Solubility tests of the parabens in PEG 4000, at various concentrations, were conducted to show the amount of binding of the parabens by PEG 4000. Dialysis tests were conducted on the other hydrophilic polymers to determine the degree of binding occurring. Results proved that the interaction of parabens with gelatin, PEG 4000, methylcellulose, and PVP was not sufficient to prohibit their use as efficient preservatives. Neither CMC nor tragacanth interacted with the parabens to any degree. Thus it was assumed that if a need for an increase in quantity of preservative arose, it could be attributed to some factor other than adsorption of the preservative by the polymer.

H. A. K. WHITNEY, JR.

STABILITY OF SOLUTIONS OF SCOPOLAMINE AND ATROPINE

Investigation into the Stability of Stock Solutions Prepared in Pharmacies, 1 comm., Simkova, A., and Haller, A., Farmacia (Czechoslovakia) 3, 3 : 81 (March) 1959.

One percent aqueous solutions of scopolamine hydrobromide and of atropine sulfate were stored under different conditions during 2 years after which the composition of the dissolved substances was studied by means of chromatography. It was found that when prepared under conditions excluding the possibility of bacterial contamination, solutions of both substances can be stored in flasks of current quality during 2 years without decomposition. The flasks are to be closed by cork and there are no other claims concerning the way of storage with exception of the one that the pH of the milieu should be lower than 4.5

HUBERT ZACEK

METHODS OF PREPARATION OF INJECTABLE SODIUM BROMIDE

About the Problem of the Production of Ampuls Containing Solution of Sodium Bromide, Beiyninson, I. D., Shulga, P. T., and Vyrshikovskaya, M. P., Meditsinskaya Promyshlennost (U.S.S.R.) 13, 4 : 47 (Apr.) 1959.

In a pharmaceutical factory in Kharkov (U.S.S.R.) a large number of ampuls containing solution of sodium bromide were rejected because opalization of the solution was observed. By the analysis of the separated precipitate that caused the opalization it was found that there were traces of iron, calcium, and magnesium, and a greater amount of aluminum. In this way it was ascertained that the sodium bromide available in the factory contained small amounts of $CaBr_2$, $MgBr_2$, $FeBr_3$, and $AlBr_3$ as impurities. These then reacted with sodium hydroxide released from the glass by hydrolysis of silicates according to the following scheme:

$$CaBr_2 + 2\ NaOH = Ca(OH)_2 + 2\ NaBr$$
$$MgBr_2 + 2\ NaOH = Mg(OH)_2 + 2\ NaBr$$
$$FeBr_3 + 3\ NaOH = Fe(OH)_3 + 3\ NaBr$$
$$AlBr_3 + 3\ NaOH = Al(OH)_3 + 3\ NaBr$$

i.e. insoluble or poorly soluble hydroxides of metals are formed. Moreover, the solubility of $Ca(OH)_2$ and $Al(OH)_3$ decreases when increasing the temperature. Another explanation of the turbidity of solutions of sodium bromide is given by the formation of insoluble silicates of metals, *i.e.*:

$$CaBr_2 + Na_2SiO_3 = CaSiO_3 + 2\ NaBr$$
$$MgBr_2 + Na_2SiO_3 = MgSiO_3 + 2\ NaBr$$
$$2\ FeBr_3 + 3\ Na_2SiO_3 = Fe_2(SiO_3)_3 + 6\ NaBr$$
$$2\ AlBr_3 + 3\ Na_2SiO_3 = Al_2(SiO_3)_3 + 6\ NaBr$$

It was found that the solution, regenerated from defective ampuls by treating the former by activated coal and then filtering, formed no more opalization after repeated sterilization. The authors have therefore solved the technological difficulty by holding the solution of sodium bromide prior to filling it into ampuls at 100°C. during 30 minutes in presence of fragments of glass capillaries (6 Kg. of glass capillaries for 500 liters of solution). After reducing the temperature activated charcoal was added and the solution was then filtered after a period of 5 minutes. This product was then treated as in the usual production of ampuls containing solution of sodium bromide.

HUBERT ZACEK

STABILITY OF DIHYDROSTREPTOMYCIN SOLUTIONS, PATENT ON

Stable Aqueous Solutions of Dihydrostreptomycin Salts, Farbenfabriken Bayer A. - G. (Fritz Ziegler, Inventor.) Ger. 936,110, Dec. 7, 1955.

Optionally buffered solutions of dihydrostreptomycin salts are mixed with phosphorus acid or its salts, bring the pH to 5-8. Thus 32.5 Gm. dihydrostreptomycin sulfate and 1.25 Gm. $Na_2HPO_3.5H_2O$ were dissolved in 75 ml. 0.25 M sodium citrate solution, the pH brought to 7 with 2N sodium hydroxide and the volume brought to 100 ml. with water.

KARL H. WOLF, CHEMICAL ABSTRACTS 53,657b

SOLUBILITY OF STEROIDS, PATENT ON

Solubilization of Pharmaceuticals, Farbwerke Hoechst A. - G. vorm. Meister Lucius and Bruning (Gustav Ekrhart and Walter Krohs, Inventors). Ger. 936,818, Dec. 22, 1955.

The solubility of pharmaceuticals, e.g., 1-phenyl - 2,3-dimethyl-S-pyrazolone, diethylallylacetamide, progesterone, deoxycorticosterone, or cortisone, is increased by addition of aqueous solutions of 1,2,4-trimethyl-3-phenyl-5-pyrazolone.

JULIUS ALTPETER, CHEMICAL ABSTRACTS 53,652 d

GLYCERIN OINTMENT, IMPROVED

An Improved Fomula For Glycerol Ointment, Horsch, W., Probst, H. And Sieler, H., Pharmazie 13:333-6, 1958 (Karl Marx Univ., Leipzig, Ger.).

An attempt was made to improve the composition and preparation as described in D.A.-B. VI. Gelatinization of starch is "regulated" by sorbitol solution and not retarded as with glycerol. The formula developed is: potato starch 6, 60% sorbitol sol'n. 20, glycerol 40, water 40, methyl p-hydroxybenzoate 0.15, ethyl alcohol 4, and finely powdered tragacanth 2 parts. The formulation permits a rapid gelatinization (5 min. heating in water bath for 100 gm. mixture.) and is non-irritating to the skin and compatible with many medicinals.

G.M. HOCKING, CHEMICAL ABSTRACTS, 53,648e

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Cost of Medications

Zugich, John J.: Hospital Pharmacy Forum: In Relation to Prescription Prices, *Am. Profess. Pharm.* 25:479 (July) 1959.

—Procedural Manuals

Latiolais, Clifton J.: Pharmacy and Procedural Manual: Policy Guide and Evaluation Tool, *Hospitals, J.A.H.A.* 33:77 (July 1) 1959.

—Purchasing

Moravec, Daniel: Beware of Pharmaceutical Garbage, *Hosp. Management* 88:73 (Aug.) 1959.

—Rational Drug Therapy

A Symposium: Drug Therapy in Hospitals, *Modern Hospitals* 95:85 (July) 1959. Includes the following articles:

Knutti, Sarah H.: How to Promote Rational Drug Therapy.

Babcock, Kenneth B.: Rx for Accreditation: Keep Drug Standards High.

Faddis, Margene O., R.N.: How Rational Drug Therapy Affects Nursing Duties.

Woodward, Marc: Industry's Role in Drug Therapy.

Bowles, Grover C., Jr.: A Pharmacist Views Drug Therapy.

PHARMACY AND THERAPEUTICS COMMITTEE

Taylor, W. I.: Pharmacy and Therapeutics Committee and the Formulary System, *Hosp. Pharm.* (Canada) 12:115 (May-June) 1959.

POISON CONTROL CENTERS

Imrie, R. J.: Poison Control Centers, *Hosp. Pharm.* (Canada) 12:118 (May-June) 1959.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Drugs; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *A.M.A. Journal* for June 6, 13 and 20.

Notice

New and Nonofficial Drugs 1959 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1959 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to January 1, 1959. The indexes listed below contain those drugs evaluated and published between December 20, 1958 and June 20, 1959.

Index

TO DRUGS EVALUATED IN THIS ISSUE

Index

TO EVALUATED DRUGS AND ARTICLES IN THE FEBRUARY, MARCH, APRIL, MAY, JUNE, AND JULY 1959 ISSUES OF THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Cottonseed Oil Emulsion — Lipomul I.V.®

COTTONSEED OIL EMULSION (Lipomul I.V.) is an emulsion of the refined fixed oil (cottonseed oil, U. S. P.) obtained from the seeds of cultivated plants of various varieties of Gossypium hirsutum Linné or of other species of Gossypium (Fam. Malvaceae).

Actions and Uses

An emulsion of cottonseed oil was introduced commercially in 1958 for intravenous use in severely malnourished patients unable to take adequate amounts of food by mouth. This preparation is marketed as a 15% oil-in-water emulsion with 4% dextrose to make it isotonic. It is nonirritaing to the venous epithelium. Hence, high concentrations of cottonseed oil emulsion may be infused intravenously. Because of this fact, and since fats as a class provide higher caloric yields per gram than either carbohydrate or protein, cottonseed oil is an excellent source of calories; 500 cc. of a 15% emulsion provides approximately 750 calories as contrasted to 100 calories with the same volume of 5% dextrose or 200 calories with a solution of 5% protein hydrolysate and 5% dextrose. Metabolic studies have indicated that this fat is utilized and that it retards the catabolic phase of metabolism, i. e., exerts a nitrogen-sparing effect.

From a nutritional standpoint, infusion of cottonseed oil would appear to be unexcelled as a means of highly effective parenteral alimentation. However, enthusiasm for such therapy must be tempered by the realization that the infusion of fat emulsions carries with it a definite risk of untoward reactions which range from very mild to quite severe. For this reason, cottonseed oil should be used with considerable discretion. It is not intended for routine use but should be reserved for patients with severe nutritional deficiency for whom other forms of parenteral feeding are inadequate to meet minimum caloric requirements, and it should be used only over a brief period of time. Logical candidates for such therapy might include patients with obstructive lesions or debilitating diseases who are being prepared for surgery, postoperative patients with temporarily nonfunctioning gastrointestinal tracts, patients with extensive burns, severely debilitated patients with traumatic conditions, and patients with severe nutritional depletion resulting from gastrointestinal disease. In occasional instances, intravenous therapy with cottonseed oil may be instituted as a temporary expedient in patients who are unable to absorb fat adequately from the gastrointestinal tract or in those with renal failure in whom maximum nitrogen-sparing is indicated. In all patients, the use of fat emulsions should be strictly limited to a brief period of time and should not exceed 14 infusions of 500 cc. each. The need should be sufficiently urgent to justify a small risk of dangerous reactions, and oral feeding should be resumed as soon as possible.

Untoward reactions to cottonseed oil emulsion may be either immediate or delayed. The immediate reactions generally occur early during the course of the initial or subsequent infusions. Delayed reactions, on the other hand, do not occur until after large amounts of fat have been infused intravenously.

The major type of immediate reaction, occurring in about 0.1% of patients, is characterized by back or chest pain, dyspnea, severe flushing, and urticaria. Chills, which may occur during an infusion or a few hours later, have been encountered in approximately 1% of patients. Intravenous fat infusions may also give rise to febrile reactions lasting a few hours; the incidence of these episodes (with temperatures of 100.6 F or over) has been about 3.5%. Immediate reactions of minor types include nausea, vomiting, abdominal discomfort, headache, mild flushing, dizziness, tachycardia, and elevation in blood pressure.

Delayed reactions to fat given intravenously are manifested by a symptom-complex sometimes called the "overloading syndrome." This syndrome is characterized by chills, fever, abdominal pain, nausea, vomiting, hepatomegaly, mild anemia, clotting defects, thrombocytopenia, and bleeding, particularly from the gastrointestinal tract. In patients with this syndrome, who have succumbed to their primary disease, pigmentation or fatty infiltration of the liver and/or spleen has been a frequent autopsy finding. The incidence of this type of untoward reaction is not known, although the likelihood of its development apparently increases as the number of intravenous infusions of fat increases. In most cases reported to date, symptoms have appeared suddenly and have gradually subsided upon discontinuance of therapy. Since the onset of the overloading syndrome may be preceded by a persistent and increased lipemia, examination of the fasting serum for residual turbidity may be a useful means of detecting impending reaction; cottonseed oil infusions should be discontinued if a gross serum turbidity (lipemia) persists for 18 to 24 hours after the last infusion. If prolonged therapy is contemplated, repeated complete hemograms should be done. Since the syndrome can occur even in the absence of gross lipemia, the patient should also be closely observed for premonitory signs and symptoms such as rising temperature, anorexia, abdominal pain, hepatomegaly, splenomegaly, and any evidence of abnormal bleeding. Liver function tests, particularly sulfobromophthalein retention, may also be helpful as an indicator of approaching intolerance. Although the available evidence indicates that effects of intravenous fat emulsions on the liver are temporary or reversible, such therapy should be undertaken cautiously in patients with severe liver disease or in those with a history of thromboembolic or other cardiovascular disease.

Dosage

Cottonseed oil emulsion is administered only by intravenous drip. It should not be mixed with blood, fluids, or any other parenteral medication or given simultaneously through the same tubing. Either one or two infusions of 250 cc. or 500 cc. each of a 15% emulsion are given each day, depending on the caloric requirements of the individual patient and taking into account the intake by other means. To minimize immediate reactions, the rate of infusion must be extremely slow. For adults, infants, and children, no more than 10 drops (0.5 cc.) per minute should be infused during the first five minutes. For the next 25 minutes, the maximum rate of infusion for adults is 40 drops (2 cc.) per minute. Thereafter, the emulsion may be infused at a rate of 100 drops (5 cc.) per minute. After the initial five minutes, the maximum rate of infusion for infants and children is one-half to one drop per pound of body weight per minute, the maximum daily dose ranging up to 10 cc. per pound of body weight.

Sufficient evidence is not at hand to permit recommending therapy with this cottonseed oil emulsion beyond the maximum of 14 infusions of 500 cc. each.

Preparation: emulsion (injection) 15% in 250 cc. and 500 cc. The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of cottonseed oil emulsion.

J.Am.Med.Assoc. **170**:135/809 (June 13) 1959

Preparations

Emulsion Cottonseed Oil (Lipomul I. V.) 15 percent; 250 ml. and 500 ml. bottles.

Vancomycin Hydrochloride Vancocin® Hydrochloride

VANCOMYCIN HYDROCHLORIDE (Vancocin) is the hydrochloride salt of an antibiotic substance obtained from strains of Streptomyces orientalis. The structural formula of vancomycin hydrochloride has not been determined.

Actions and Uses

Vancomycin hydrochloride, introduced in 1958, is an antibiotic which is highly active against gram-positive cocci. The drug is bactericidal, in vitro and in vivo, for streptococci, pneumococci, and staphylococci. Vancomycin is excreted in the urine; its metabolic fate and distribution are not known.

Vancomycin hydrochloride administered intravenously has proved to be valuable for the treatment of certain severe staphylococcic infections. In a number of instances, it has undoubtedly been lifesaving. The drug is not intended for routine use, nor should it be used in mild infections. Instead, it should be reserved for critically ill patients with life-endangering infections produced by strains of staphylococci which are resistant to the antimicrobial action of the commonly used antibiotics. Because of the specificity of vancomycin against such infections, it is particularly valuable for use in hospitals in which so-called antibiotic-resistant staphylococcic infections are becoming an increasingly serious problem. To date, no instance of natural or acquired staphylococcic resistance to vancomycin has been reported, either in vitro or in vivo. Neither has cross resistance to other antibiotics been observed. If, in the light of subsequent clinical experience, all strains of the organism remain uniformly susceptible to vancomycin, this antibiotic may well become the drug of choice for the treatment of severe staphylococcic infections which fail to respond to other antibiotics. The indiscriminate use of vancomycin is, in large measure, discouraged by the fact that it must be administered intravenously.

Vancomycin hydrochloride has also been used in the treatment of severe infections produced by penicillin-resistant strains of alpha or nonhemolytic streptococci. In a number of patients with subacute bacterial endocarditis due to such organisms, the drug has produced gratifying results. There appears to be little justification for its use in beta hemolytic streptococcic or pneumococcic infections since these invariably respond well to therapy with penicillin.

The toxicity of vancomycin hydrochloride is minimal for most short-term therapy. The drug can, however, produce an impairment of auditory acuity, especially when therapy is prolonged or when large doses are given. In the presence of severely impaired renal function, the excretion of vancomycin is decreased and the drug accumulates in the blood. Since this may enhance the likelihood of ototoxicity, the drug should be used with considerable caution in patients who have renal damage. Periodic determinations of the blood urea nitrogen level are likewise suggested for all patients receiving doses greater than 2 Gm. per day. Vancomycin hydrochloride is irritating to the venous endothelium and may cause pain at the site of intravenous injection; chemical thrombophlebitis has been observed when concentrated solutions were used or when the drug was administered repeatedly into the same vein. Macular skin rashes and febrile reactions have been encountered.

Dosage

Vancomycin hydrochloride is administered only by the intravenous route. For adults, the usual dose for a 24-hour period is 2 Gm. This is generally administered in amounts of 500 mg. every six hours, although some investigators have found it feasible to give only two infusions of 1 Gm. each at 12-hour intervals. Higher doses of 3 to 4 Gm. daily should be used only in desperately ill patients who have normal renal function. The daily dosage for children is 20 mg. per kilogram of body weight.

Concentrated solutions of the drug, containing 500 mg. in 10 cc., can be given by direct intravenous injection over a period of four to five minutes. Preferably, however, this concentrated solution should be diluted with 100 to 200 cc. of isotonic sodium chloride solution or 5% dextrose in water for injection and infused by intravenous drip over a period of 20 to 30 minutes.

Preparations: solution (injection) 500 mg. in 10 cc.

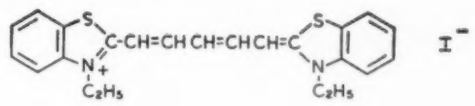
Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of vancomycin hydrochloride.
***J.Am.Med.Assoc.* 170:136/810 (June 13) 1959.**

Preparations

Injection Vancomycin (Vancocin) Hydrochloride 0.5 Gm.

Dithiazanine Iodide Abminthic® Iodide Delvex® Iodide

DITHIAZANINE IODIDE (Abminthic, Delvex) is 3-ethyl-2-[5-(3-ethyl-2-benzothiozolinylidene)-1,3-pentadienyl]benzothiazolium iodide.—The structural formula of dithiazanine iodide may be represented as follows:



Actions and Uses

Dithiazanine iodide, introduced commercially in 1958, is a blue cyanine dye which is used clinically as an anthelmintic. The drug possesses an amidinium ion system, a distinctive chemical configuration characterized by a quaternary nitrogen separated from a tertiary nitrogen by a resonating or conjugated carbon chain of alternate double and single bonds; this resonating amidinium ion system is apparently essential for anthelmintic activity. Cyanine dyes as a class are sparingly soluble and poorly absorbed from the gastrointestinal tract. The high levels in the intestine after oral administration of dithiazanine exert an inhibitory effect on the anaerobic metabolic reactions of certain intestinal helminths, thereby producing a chemotherapeutic effect against susceptible parasites.

Dithiazanine is highly active against Trichuris trichiura (whipworms) and Strongyloides stercoralis. Cure rates ranging from 72 to 100% have been reported in trichuriasis and from 62 to 100% in strongyloidiasis. The drug is far more effective than previous modes of therapy in either of these worm infestations, i. e. hexylresorcinol retention enemas for Trichuris organisms and intravenously administered gentian violet for Strongyloides infections. In responsive patients, therapy with dithiazanine effects a cure rather than merely removing most of the worms. Hence, it is considered the drug of choice for the treatment of trichuriasis and strongyloidiasis.

Dithiazanine is about as effective as piperazine for the treatment of pinworms (Enterobius vermicularis) and roundworms (Ascaris lumbricoides). Since the use of dithiazanine is associated with a much higher incidence of gastrointestinal side-effects than is therapy with piperazine, the latter agent is considered preferable for these infestations. Therapy with dithiazanine for pinworms or roundworms should be reserved for those patients in whom a course of treatment with piperazine has failed to eradicate the parasites. However, dithiazanine should prove to be highly useful as a single agent for the treatment of multiple worm infections, such as ascariasis and trichuriasis, which frequently occur in the same patient.

Dithiazanine, used alone or in combination with tetrachloroethylene, has been tried for the treatment of hookworm infections due to Necator americanus. Although the preliminary clinical trials have suggested some degree of chemotherapeutic effectiveness, the drug appears to be inferior to

tetrachloroethylene for this purpose. Hence, its use in hookworm infections is considered experimental. There is, likewise, inadequate evidence to establish the usefulness of dithiazanine in dwarf tapeworm (Hymenolepis nana) parasitism.

Serious toxicity has not been encountered during the clinical trials of dithiazanine, an effect attributable to its almost complete lack of absorption from the gastrointestinal tract. The drug does, however, exert a local irritant effect on the gastrointestinal mucosa. Thus, nausea, vomiting, and anorexia occur frequently; abdominal cramps and diarrhea may also be encountered. For this reason, the drug is probably best administered with meals. Since cyanine dyes as a class are highly toxic when given parenterally, dithiazanine should not be given in any condition in which its gastrointestinal absorption might conceivably take place. In view of past experience that other cyanine dyes can cause kidney damage, dithiazanine should be used cautiously in patients with renal disease. The drug is obviously contraindicated in any condition that may be aggravated by vomiting.

Dosage

Dithiazanine iodide is administered orally. The optimal daily dose is 45 mg. per kilogram of body weight (20 mg. per pound) with a maximum daily dosage of 600 mg., administered in three divided doses, for 5 to 10 days in trichuriasis, for 5 days in ascariasis and enterobiasis, and for 7 to 21 days in strongyloidiasis.

Preparations: tablets 50, 100, and 200 mg.

Eli Lilly and Company cooperated by furnishing scientific data to aid in the evaluation of dithiazanine iodide.

J.Am.Med.Assoc. **170:131/675 (June 6) 1959.**

Preparations

Capsules Dithiazanine (Abminthic) Iodide 0.2 Gm.
Tablets Dithiazanine (Delvex) 50 mg., 0.1 Gm., and 0.2 Gm.

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. KAUTZ, M.D., *Secretary*

Current Status of Therapy in Glomerulonephritis

LOWELL A. RANTZ, M.D., *San Francisco*

The term glomerulonephritis is applied to inflammatory diseases of the renal glomeruli. Acute and chronic or latent stages may be recognized clinically and anatomically.

Acute Glomerulonephritis

Acute glomerulonephritis is a disorder associated with the appearance of protein, erythrocytes, leukocytes, and renal tubular epithelial cells in the urine. Red blood cell casts may be present and serve to distinguish the disease sharply from others in which bleeding occurs distal to the glomerulus. The full blown clinical picture is completed by the addition of hypertension, edema, oliguria, azotemia, and, in the more severely ill, cardiac enlargement with or without congestive failure. Convulsions occur in a very few cases.

Nearly all illnesses exhibiting this pattern, and a high proportion of all others in which glomerular bleeding occurs, are the result of group A hemolytic streptococcus infection. Only a few strains of these organisms, notably those of types 4, 12, and 49 (Redlake), are able to produce this disease. The usual sequence of events includes a streptococcic respiratory infection, which may be mild or clinically inapparent, followed by a period in which the individual recovers and seems well. Nephritis develops two to three weeks after the initial illness. A considerable number of cases arise as complications of streptococcic pyoderma.

Glomerulitis may occur in a variety of other conditions including polyarteritis nodosa, disseminated lupus erythematosus, and others of the collagen diseases, in hypersensitivity states and drug reactions, in bacterial endocarditis, and, in certain cases, without a definable precipitating disease. The establishment of an etiological diagnosis is essential for the determination of the prognosis. Poststreptococcic nephritis has a striking tendency to recovery, whereas many of the other types may be expected to have a protracted course. Not infrequently the clinical evidence of a renal lesion will call attention to a generalized disorder that may even lead to death.

Assessment of the prognosis and results of treatment in glomerulonephritis is also complicated by the fact that exacerbations of the chronic form of the disease may be clinically indistiguishable from the acute stage and may also have occurred after a streptococcic infection. In these instances improvement may occur, but complete healing is not to be expected.

Culture of the nasopharynx before any antimicrobial therapy is administered and determination of the serum antistreptolysin O titer are essential diagnostic studies in patients with renal bleeding. The isolation of group A streptococci or an antistreptolysin titer of 250 units per milliliter or more increases the probability that the disease is a poststreptococcic nephritis. An antibody level of 100 units per milliliter or less excludes this possibility and indicates the need for a careful search for one of the other causes of this syndrome.

Treatment of Poststreptococcic Nephritis

Clinical Course and Prognosis.—A very few patients with poststreptococcic nephritis die within days or weeks of the

From the Department of Medicine, Stanford University School of Medicine.

onset of the disease as the result of acute persistent renal failure. This sequence of events should always suggest another diagnosis such as polyarteritis nodosa or bacterial endocarditis. Continuing subacute activity with a progressive decline in renal function and death within a year characterizes another small group (not over 5% of all cases). Some of these doubtless represent examples of exacerbation of a previously unrecognized chronic nephritis.

About 10% of patients with poststreptococcic nephritis have been said to enter a chronic or latent phase characterized by the presence in the urine of protein and erythrocytes in small amounts and numbers. This phase may persist for years before deterioration of kidney function supervenes. Few serial studies have been made of acute nephritis of proved streptococcic origin. Recent investigation of this disease in young adults suggests that latency is extremely uncommon and that complete healing nearly always occurs.

It has often been stated that the chronic nephritis, which is discovered in persons in whom no history of an acute illness may be obtained, has followed poststreptococcic nephritis that escaped clinical recognition. This point of view may be altered in the future if the frequency of healing of definite streptococcic nephritis proves to be greater than has been supposed.

These considerations require a reevaluation of the prognosis in streptococcic nephritis. It is proper to assume a most optimistic position. Less than 5% of all patients will go rapidly into acute or subacute progressive renal failure, with death in days to months after onset of the disease. Nearly all of the remaining patients will recover, although healing may require one to two years.

Antimicrobial Therapy.—Substantial evidence exists which indicates that persistence of group A streptococci in the tissues of the pharynx is intimately concerned with the pathogenesis of rheumatic fever after a streptococcic respiratory infection. It is now agreed that these organisms should be eradicated by administration of antibiotics when treatment of this disease is instituted. Similar information pertaining to glomerulonephritis is not available, but this procedure is safe and sensible, particularly since the carrier of nephritogenic streptococci is a major health hazard. Even though hemolytic streptococci are not demonstrable in a throat culture, small numbers of these organisms may be present and escape detection. Penicillin is the agent of choice and should be administered in one of three ways: (1) benzathine penicillin G (Bicillin, Permapen), 900,000 to 1,200,00 units intramuscularly as a single dose; (2) buffered potassium penicillin G (Dramcillin, Penalev, Pentids) or phenoxymethyl penicillin (Pen-Vee, V-Cillin), 125 mg. (200,000 units) to 250 mg. (400,000 units) four times daily for two weeks by mouth; or (3) procaine penicillin G (Crysticillin, Depo-Penicillin, Diurnal Penicillin, Lentopen), 300,000 units intramuscularly daily for two weeks.

Continuous chemoprophylaxis to prevent subsequent group A hemolytic streptococcic infections is essential in the management of patients with rheumatic fever and rheumatic heart disease. Its value in glomerulonephritis is less well defined. Specific immunity to the casual nephritogenic streptococcus in acquired after infection, and it is highly unlikely that the individual will come in contact with another strain with nephrotoxic properties. Nevertheless, it has been demonstrated that infection by hemolytic streptococci is the most common cause of exacerbation in chronic nephritis. It would seem desirable to protect the patient against these organisms while healing of the acute lesion is in progress. This can be accomplished by the administration of 1,200,000 units of benzathine penicillin G given intramuscularly at monthly intervals for six months. Oral therapy with either penicillin or sulfonamides is not recommended because it is less reliable and because the regular follow-up examinations required during this interval permit the ready establishment of a parenteral prophylactic regimen.

Serious allergic reactions, including fatal anaphylaxis, may follow the use of penicillin in any person but are most common in those individuals who have received the drug before. Every effort must be made to avoid the administration of penicillin to individuals who have previously had an allergic reaction to this drug. Those who present a history of such a reaction should receive eradicatory therapy with full doses of erythromycin (Erythromycin, Ilotycin), and the prophylactic regimen should be omitted.

Rest.—The importance of restriction of activity in the treatment of streptococcic glomerulonephritis has not been determined but should be enforced, not only during the initial stages but also later, in the hope that chronicity may be avoided. Most of the patients are children, and complete bed rest cannot be maintained over a long period of time without causing needless emotional disturbances.

Those who are quite ill wtih edema, hypertension, or cardiac failure should rest quietly in bed until the diuretic phase of recovery has passed. This usually requires only a few days. Hospitalization should be avoided unless the nature of the illness indicates that special therapeutic measures may be required. After this period, both in severe and in mild cases, the patient should be confined to the house and immediate environs and should assume a bed and chair existence, with a minimum of physical activity. This regimen should be maintained until healing has occurred or until it becomes evident that further progress will be slow.

Certain patients still exhibit proteinuria and hematuria one to two months after onset of the disease. Healing in these individuals may require several additional months, but it is not desirable to maintain the degree of rest that has been described throughout this period, nor is it known to be advantageous. A gradual increase of activity in this small group of patients is appropriate. The urine should be examined frequently and a strict regimen reinstituted if a definite increase in hematuria or cylindruria occurs.

Diet.—Restriction of fluids to 700 cc. more than the combined total of urine and vomitus, and of sodium to less than 300 mg. per day, is mandatory in patients with edema and oliguria. During the period when these manifestations of nephritis are present, the diet should be high in carbohydrate and low in protein and potassium. After the diuretic phase has passed, edema is gone, and blood pressure is normal, a regular diet may be resumed and fluids given freely. Reduction of protein in the diet has been stressed by some as an important therapeutic measure in acute nephritis, but evidence that this procedure will promote healing or lessen the frequency of chronicity is lacking. An excessively high-protein intake should be avoided. Approximately 1 Gm. per kilogram of body weight per day is an appropriate amount.

Drug Therapy.—Adrenal corticosteroids (glucocorticoids) do not alter the course of the disease and should not be used. Sedatives may occasionally be necessary to control restlessness and anxiety and, rarely, are used in larger amounts as anticonvulsant agents.

Special Situations

The simple measures described will suffice in most cases of streptococcic nephritis. A small proportion of patients exhibit manifestations of the disease that require special attention.

Severe Oliguria.—Severe and persistent oliguria or anuria must be managed with care, since overhydration may be fatal. Management is precisely like that for any other form of acute renal failure. Fluids should be limited to 700 cc. more than the combined total of urine and vomitus. This entire amount of liquid is best administered intravenously over a 24-hour period as a 20% solution of dextrose injection. The patient should, if possible, be weighed daily on a good scale, and fluid intake should be so adjusted that a little loss of weight occurs each day.

Since hyperkalemia is the most serious complication of prolonged oliguria, frequent measurement of the serum electrolyte levels is necessary. When hyperkalemia appears, an effort should be made to reduce the total body store of potassium by the administration of an ammonium carboxylic ion exchange resin. This should be given by mouth in a daily dose of 50 Gm. (smaller amounts are appropriate for children) suspended in sweetened water. In the presence of vomiting, a 10% suspension may be administered as a retention enema and removed after a few hours.

The use of the artificial kidney, if available, must be considered if diuresis does not begin before azotemia and hyperkalemia become severe, in spite of proper medical management. The indications and techniques for the application of this device are beyond the scope of this review.

Congestive Heart Failure.—Digitalis may be used in the treatment of congestive heart failure during the course of acute nephritis, but diuretics are contraindicated. No special therapy is ordinarily necessary. If symptoms are severe, a phlebotomy may be performed profitably, withdrawing 7 to 10 cc. of blood per kilogram of body weight. Careful restriction of sodium intake from the onset of the illness will minimize the possibility that congestive heart failure will appear.

Convulsions.—A few patients with acute nephritis exhibit severe hypertension and convulsions in spite of careful management and restriction of sodium intake. In the past, magnesium has been given parenterally for the control of the convulsive state and for the reduction of blood pressure under these circumstances. This is a hazardous procedure, since these patients have markedly diminished renal function, and overdosage of magnesium, with serious toxicity, is likely to occur. The intramuscular injection of a combination of hydralazine (Apresoline) hydrochloride (0.10 to 0.15 mg. per kilogram of body weight) and reserpine (Raudoydin, Raurine, Rau-Sed, Reserpine, Reserpoid, Roxinoid, Sandril, Serfin, Serpasil, Serpate, Serpiloid) (0.15 mg. per kilogram of body weight) is an effective nontoxic method for reducing the hypertension of nephritis. The effect on blood pressure occurs within 20 minutes and is long lasting so that only a single injection each day is necessary. Side-effects are rare and consist of mild nausea, faintness, postural hypotension, and moderate tachycardia.

Chronic Nephritis

Chronic or latent glomerulonephritis does not require treatment until hypertension and its complications, or renal failure, appear. Drugs to reduce blood pressure must be used with caution in patients with glomerulonephritis so that renal failure will not be precipitated or enhanced. These agents, particularly those that block the sympathetic ganglions, should be reserved for those cases in which rapid deterioration of vision and cardiac or renal function seems to be directly related to the hypertension.

No treatment is known to be of great help when progressive loss of renal function leads to the clinical manifestations of uremia. A low-protein diet and careful attention to the intake of fluids and electrolytes will prolong useful life, but the process is inexorable.

The anemia of chronic renal failure is usually not severe, and its correction by blood transfusion does not often contribute to the well-being of the patient. Furthermore, reactions may occur, particularly if blood is administered on several occasions, and may lead to serious deterioration of renal function. For these reasons, administration of washed red blood cells should be avoided unless the anemia is unusually severe and clearly contributes to some aspects of the patient's illness. The use of whole blood, even under these circumstances, is too hazardous. Blood should never be administered as a "tonic" in an attempt to improve the general state of well-being of the usual patient with chronic nephritis and renal failure.

Nephrotic Syndrome

Several forms of renal disease may be associated with the nephrotic syndrome. It is not certain at the present time whether it is often, if ever, a complication of a chronic poststreptococcic nephritis. The prognosis undoubtedly depends on the pathogenesis of the underlying disturbance of the kidney. The recognition of the various forms and the management of some with adrenal steroids cannot be considered here.

J.Am.Med.Assoc. 170:122/948 (June 20) 1959.

Report to the Council

The Council has authorized publication of the first paper presented as part of a symposium and panel discussion on the Use and Abuse of Adrenal Steroids, together with introductory comments by the chairman-moderator of the program, Dr. Thomas McPherson Brown. The program, sponsored by the Council with the cooperation of the George Washington University School of Medicine and the Medical Society of the District of Columbia, was held at the Lisner Auditorium of the University in Washington, D. C., on Sept. 25, 1958.

H. D. KAUTZ, M.D., *Secretary.*

The Use and Abuse of Adrenal Steroids

It is well known that the adrenal steroids can cause a variety of complications, some of which are mild and reversible and others more serious and, at times, irreversible. An awareness that side-effects from various drugs must be anticipated has always been a familiar aspect of medical practice. Most physicians have assumed, quite naturally, that the problems posed by the adrenal steroids are similar to those encountered with other drugs. It is now apparent, however, that the adrenal steroids have created a number of new effects and considerations which have not been experienced in the past.

One of the most important aspects of toxicity from the steroids is interference with the natural defense mechanisms of the body during the period when symptomatic relief may be observed. Complications associated with alterations in the immune mechanism are particularly serious because of their insidious and obscure nature. A reduction in host resistance may mask the spread of infection from a previously controlled but unknown focus. In a similar manner, an unrecognized tendency for the development of peptic ulcers may be stimulated by adrenal steroids, and symptoms usually associated with this complication may be suppressed. Such ulcers can progress to hemorrhage or perforation without warning symptoms which would otherwise suggest their presence. These and other complications such as induced adrenal cortical insufficiency, demineralization of bone and collapse of vertebrae, and the transformation of rheumatoid vasculitis into necrotizing arteritis, with the clinical pattern of the disseminated lupus erythematosus or polyarteritis nodosa, provide additional evidence of the unique nature of the medical problems created by the adrenal steroids. General awareness of these matters has been limited, as evidenced by the widespread use of the adrenal steroids for treatment of relatively minor medical conditions.

J.Am.Med.Assoc. 170:125/951 (June 20) 1959.

Endocrine Disorders — Steroid Therapy in

Steroid Therapy In Endocrine Disorders

JOHN E. HOWARD, M.D., *Baltimore*

Mine is perhaps the easiest of the subjects on today's program with which to deal. Administration of adrenal steroids to patients with endocrine disorders is almost invariably "replacement" therapy; and, if one adopts a simple philosophy that nature is almost always right, the problem becomes one of imitating nature as closely as one can. In other words, the effort is to provide the organism with the same quality of steroid hormones which the adrenals could have and would have delivered had their mechanisms been intact. I shall develop my thesis along these lines and later perhaps point out some situations in which this philosophy may perhaps be inadequate or less than optimal.

There is excellent reason for believing that under normal conditions the adrenal glands secrete into the circulation approximately 25 mg. of hydrocortisone each 24 hours, and of aldosterone, the equivalent in desoxycorticosterone acetate of 1 to 2 mg. The derivation of these two approximate figures is based on (1) the quantitative urinary output of degradation products of these compounds in normal persons, (2) comparable outputs in adrenalectomized patients to whom 25 mg. of cortisone and 1 to 2 mg. of desoxycorticosterone acetate have been given, and (3) the excellent state of well-being constantly produced in patients with uncomplicated adrenal insufficiency.

For simplicity and to avoid semantic and mathematical minutiae which would greatly detract from the main issues, I shall outline replacement therapy only in terms of desoxycorticosterone (Cortate, Decortin, Decosterone, Doca, Percorten) acetate and cortisone (Cortisone, Cortogen, Cortone) acetate. So far as I am aware, more recent synthetic corticosteroid compounds have approximately the same potency relative to cortisone when used as replacement therapy as when used as anti-inflammatory agents; i. e., prednisolone (Delta Cortef, Hydeltra, Meticortelone, Paracortol) and prednisone (Deltasone, Deltra, Meticorten, Paracort) per milligram are about five times as potent as hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) and cortisone. Certain other still newer compounds have about twice the potency of prednisone, and all have the deleterious side-effects in roughly the same proportions.

Adrenal Cortical Hypofunction (Addison's Disease)

Let us begin with a patient with adrenal cortical hypofunction (Addison's disease), whose adrenals have been rendered functionally inadequate by idiopathic atrophy, tuberculous invasion, cancer, or hemorrhage. As with the diabetic, one usually sees for the first time the patient with adrenal cortical hypofunction severely ill from some complication which has brought his condition acutely to a state of crisis or near crisis. I shall mention this later, but now let us prescribe for the patient who has noted browning of the skin, weakness, a little weight loss, and fall in blood pressure in whom laboratory studies are entirely corroborative and in whom no complications exist. One can at once perscribe 2 mg. of desoxycorticosterone acetate daily intramuscularly and 12.5 mg. of cortisone orally after breakfast and supper, with every confidence that he or she will feel nearly normal within one to two weeks and will soon thereafter have regained the lost weight and strength. So efficacious is this therapy that one may confidently predict to the patient that he will feel as well as ever and be able to carry on all his usual activities; I honestly believe that, given the necessary choice, one would today rather be afflicted with adrenal cortical hypofunction than with diabetes mellitus.

The requirement of 1 to 2 mg. of desoxycorticosterone acetate or some other primarily sodium-retaining corticosteroid such as fludrocortisone (Alflorone, F-Cortef, Florinef) acetate in addition to cortisone seems almost uniformly agreed on. There may be a rare patient with adrenal cortical hypofunction in whom cortisone alone will suffice for optimal therapy, but in the department of medicine at Johns Hopkins University School of Medicine we have not seen such a one. Indeed, the commonest finding among patients who have been treated elsewhere without good results is that replacement therapy has been attempted with cortisone alone. A dose of 50 or even 75 mg. of cortisone has been used each day; the patient has not felt well, and signs and symptoms of hyperadrenocorticism have appeared, perhaps because patients with endocrine deficiencies are notoriously sensitive to the products they lack. Excellent well-being is soon established when small doses of desoxycorticosterone acetate are given and the cortisone is reduced to 12.5 mg. twice daily.

The mechanics of administration of these compounds should be mentioned. For simplicity, cortisone acetate given orally is to be preferred, and, despite the fact that the time of action is supposed to last but six or eight hours, patients have uniformly done well on half a tablet (12.5 mg.) taken after breakfast and supper. Cortisone (or hydrocortisone) acetate given intramuscularly is a cumulative drug, potential hormone being yielded slowly to the circulation but for prolonged periods of time. It is, therefore, useless for quick efficacy; but for stupid or incapacitated patients with adrenal cortical hypofunction, Dr. Segaloff states he found that single injections of 250 to 300 mg. every two weeks yield satisfactory replacement.

Our patients have uniformly been started on therapy with desoxycorticosterone acetate given intramuscularly, and most of them become so used to a morning injection that they prefer to continue on such a regimen, administering it to themselves. Good results may be obtained with depots of desoxycorticosterone acetate, either by pellet implantation (now largely out of fashion) or by the long-acting compound, desoxycorticosterone (Percorten) trimethylacetate, which may be given once per month intramuscularly in the same dosage that one would have given daily, i. e., 60 mg. if the daily dose had been 2 mg. Good results have also followed the use of a daily oral dose of 0.1 mg. of fludrocortisone acetate which substitutes approximately for the sodium-retaining activity of 2 mg. of desoxycorticosterone acetate. On all these regimens the patient's palate is permitted to regulate his intake of table salt.

Patients with Adrenal Cortical Hypofunction Under Stress

When the normal person is placed under metabolic stress as by infection, broken bone, surgical operation, or the like, he responds by a greater output of adrenal corticosteroids. With a small stress he may double the usual quantity secreted; with a major castastrophe 100 mg. or perhaps more of hydrocortisone will be provided per 24 hours. This increased corticosteroid production seems purposive and useful, for the

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patient with adrenal cortical hypofunction, when under such stress, goes into adrenal insufficiency unless increased dosage of replacement is provided. The theoretical concept involved is much like that for the person with a mild case of the disease before the days of cortical hormones—he had just enough hormone to keep going, perhaps with added salt, but mild trauma of even a minor surgical procedure or a general anesthetic inevitably resulted in death.

So when the well-regulated patient gets an infection or requires a surgical procedure, one raises the dose of corticosteroid (added sodium-retaining hormone is not necessary) to meet the requirements; in a mild attack of influenza one would give 50 mg. of cortisone acetate daily for the duration of the illness; for a major infection like lobar pneumonia or meningococcus meningitis, 100 mg. per day. In illnesses with vomiting or diarrhea and with surgical procedures, it is well to provide parenteral replacement therapy, recalling always that cortisone acetate given intramuscularly is slowly absorbed; therefore, for quick effectiveness one must use soluble hydrocortisone sodium succinate (Solu-Cortef) given intravenously, in comparable doses and spacing of such dosage as defined for the oral preparations.

Crisis of Adrenal Insufficiency

Acute adrenal insufficiency, so-called crisis, may arise, of course, in the patient with previously unrecognized disease and may also occur in the treated patient who sustains an acute trauma which has deprived him of his usual dosage. Now crisis is seen fairly commonly in patients who have been taking corticosteroids as therapeutic agents (and have consequent adrenal atrophy) and who have suddenly been deprived of their drugs. When insufficiency of any degree has existed for even a few hours, much more hormone is needed to restore normal function than would have been needed to prevent the situation from arising in the first place. This is not unlike the need for huge doses of insulin required to bring certain patients out of diabetic coma. As much as 300 mg. or more of hydrocortisone may be needed in 24 hours until acute manifestations have been controlled, and, with the circulatory collapse which usually accompanies adrenal insufficiency, it is almost always requisite to provide the therapy intravenously, together, of course, with other indicated adjuvant measures such as transfusions to maintain blood volume, saline solution for hydration, and glucose. When the crisis has passed, gradual lowering to maintenance doses of corticosteroid is in order. Current information indicates that the total water deficit is not so great as we previously had thought, and that intercompartmental shifts have made water deficit more apparent than real. Hence, we now no longer use the huge quantities of isotonic sodium chloride solution (10 to 15 liters) that we once did, which were likely to result in overhydration and late appearance of edema.

An example may be cited to stress the speed with which one must act in adrenal crisis. A patient with rheumatoid arthritis had been taking 100 mg. of cortisone per day for two years. She contracted lobar pneumonia, and, with her initial chill, she vomited. This occurred at noon, just after the midday dose of cortisone had been taken. She was hospitalized, and antibiotic therapy was begun within two hours of the chill. In the hustle and bustle of these therapeutic measures, the rheumatoid arthritis and cortisone were forgotten. At 10 p.m., though all had seemed to be going well, the patient suddenly became weak, blood pressure fell to very low levels, pulse rose, and shock was serious. A dosage of 100 mg. of soluble hydrocortisone was given intravenously over the next four hours by the wise physicians, who recognized at once the nature of the problem, and by the next morning all was well again. In all likelihood the patient would have been dead by morning had these measures not been used .

Pituitary Insufficiency

Since the adrenal cortex is dependent on adrenotropic hormone of the pituitary and adrenal atrophy occurs in its absence, the problem of steroid replacement therapy in panhypopituitarism is almost identical with that of primary adrenal insufficiency. However, aldosterone secretion does not seem to be under pituitary control, and under most conditions no sodium-retaining hormone need be given. For corticosteroid therapy, one follows the same principles laid down for the treatment of the patient with adrenal cortical hypofunction.

Adrenal Cortical Hyperfunction (Cushing's Syndrome), Adrenalectomy, and Operations on the Pituitary Gland

When one intends to remove a tumor, or totally or subtotally excise the adrenals for adrenal cortical hyperfunction (Cushing's syndrome), plans must be laid to deal with the temporary or permanent adrenal insufficiency which is bound to follow. Because abdominal difficulties such as distention make it unlikely that the patient can take oral feedings for several days, intramuscularly given depot cortisone acetate is the therapy of choice. To build up the blood level, therefore, to approximate delivery of 100 mg. of cortisone per day to the circulation, 100 mg. is given intramuscularly for two or three days prior to the operation, and this procedure is continued during the period of maximal operative stress—two to four days postoperatively. The dose is then reduced to meet the needs of the particular situation. If total adrenalectomy has been performed, replacement will have to be continued for life, and desoxycorticosterone also must be administered just as to the patient with adrenal cortical hypofunction. However, in those patients who have been adrenalectomized for adrenal cortical hyperfunction, more than the usual replacement dose of corticosteroids is needed and usually for long periods of time. Rarely can one achieve optimal results with less than 50 mg. of cortisone per day. Perhaps the tissues have become accustomed to large doses of circulating hormone during the time of adrenal cortical hyperfunction and now need more than does the normal tissue. With removal of a tumor or after subtotal adrenalectomy, the remaining adrenal tissue usually takes over in a few days or weeks, and desoxycorticosterone is not needed. The tapering of the corticosteroid dosage to such patients is a very delicate procedure and must be done with utmost care. For sometimes after removal of a tumor the atrophic adrenal does not resume function, probably from failure of the pituitary to secrete corticotropin, and the patient will then be dependent on extraneous corticosteroid for life. Permanent adrenal insufficiency also occasionally follows subtotal adrenalectomy when the surgery inadvertently causes necrosis of the remaining adrenal tissue.

A word should be said about corticosteroid therapy in thyroid abnormalities, especially hypothyroidism. If the myxedema has resulted from pituitary disease, there is, of course, likely to be adrenotropic hormone deficiency too, leading to adrenal atrophy. When one gives thyroid hormone to such a patient, the added metabolic burden may make manifest the adrenal inadequacy and provoke an adrenal crisis. Patients have died from this series of events. Even with primary hypothyroidism, i. e., originating in disease of the thyroid and with an intact hypophysis, the adrenals may be functionally inadequate; perhaps they, too, have myxedema as suggested by Dr. Howard Means. In any event, it is a good precaution to provide replacement of corticosteroid to severely myxedematous persons when thyroid therapy is begun. One can find out later by tapering the dose whether it will or will not be permanently needed.

There is a converse to this story, too. We have concluded that corticosteroid therapy to the thyroid-deficient patient is quite dangerous, having now seen three persons develop acute psychopathic disorders within the first few days of normal replacement corticosteroid dosage. It would seem desirable, therefore, to be sure of reasonable levels of thyroid hormone when steroids are to be given.

It should be recalled that degradation of corticosteroids is much slowed in thyroid deficiency, as it is in severe liver disease. The step from hydrocortisone to the tetrahydro form cannot be normally carried out; hence, glucuronidation and excretion are delayed. We observed and reported production of full-blown adrenal cortical hyperfunction in a patient with panhypopituitarism to whom only normal replacement doses of cortisone were given, 25 mg. four times daily, but whose thyroid deficiency was not treated. All symptoms and signs of hyperadrenocorticism disappeared when thyroid was given, despite continuance of the same dose of cortisone.

Summary

In a limited discussion of this kind, one cannot take up all the possible variations which may be met in an individual case. An attempt has been made to outline certain principles which may guide one's actions. These simple principles seem soundly based on theoretical and experimental grounds, and, most important, they have proved to be highly successful in practical use at the bedside. There are those who tell us we have too great a faith in Mother Nature and that we undertreat our patients when we follow the precepts I have outlined. The answer is that it works, and our surgical colleagues tell us that they cannot tell the operative or postoperative course of patients so managed from that of the normal individual under similar circumstances. I would agree, however, in acute situations, to err on the side of too much, rather than too little, and, when there is doubt, give more rather than less replacement therapy.

Since the advent of readily available adrenal steroids, they have been used in an effort to counteract circulatory collapse in all sorts of circumstances. It is true that acute adrenal insufficiency sometimes occurs from adrenal hemorrhage and, judging from histological appearance, may exist in fulminating infections of various types. There is usually no fault to find with administering corticosteriods to such patients in the hope that such adrenal insufficiency is indeed their transient problem. However, let not the availability of corticosteroids and the hope that their administration will be efficacious make us lazy and sloppy clinicians. Usually in such instances postmortem examination has shown the presence of an unsuspected internal hemorrhage, or a silent coronary occlusion, or the like. It must be rare indeed for shock of adrenal origin to arise unsuspected in a patient who has had an accurate case history taken and a thorough physical examination.

J.Am.Med.Assoc. 170:126/952 (June 20) 1959.

POSITIONS

in hospital pharmacy

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PERSONNEL PLACEMENT SERVICE

The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the *Minimum Standard for Pharmacies in Hospitals.* A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the AMERICAN JOURNAL OF HOSPITAL PHARMACY without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown below, including the code number.

Address all inquiries to

Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington, 7, D. C.

positions wanted

PHARMACIST—Male, married. B.S. Three years' experience in Sudan Interior Mission Hospital. Prefers to locate in South particularly S.C. Registered in S.C. PW-183

STAFF OR ASST. CHIEF PHARMACIST—Female, single. B.S. Three years' hospital experience. Prefers to locate in Midwest, registered in Mo. PW-181

PHARMACIST—Male, married. B.S. Interested in career in hospital pharmacy. Prefers to locate in East. Registered in N.Y. and Ill. PW-180

CHIEF PHARMACIST—Male, single. B.S. Four years' hospital experience. Interested in manufacturing and administration. Registered Conn. Prefers Northeast section of country. PW-179

PHARMACIST—Male. B.S. received 1958. Married. Prefers western part of country. Registered Colorado. PW-178

ASST. CHIEF OR CHIEF PHARMACIST—Male. B.S. received in 1954. Desires to locate in Mich., Ohio or Ill. Registered Mich. PW-177

ASST. CHIEF OR STAFF PHARMACIST—Female, single. B.S. Registered in La. and Ohio. Prefers Ohio and Northern part of country. PW-176

PHARMACIST—Female, single. Graduate of University of Nebraska. B.S. Registered in Nebr., Mich. and Pa. PW-175

CHIEF PHARMACIST—Male, married. B.S. Registered in Mo. and Kansas. Prefers Southeast or Southwest section of country. Desires position with possibility of assuming administrative duties. PW-174

PHARMACIST—Butler University graduate with Ph.C. degree; registered in Ill., Ky., Ind., Ore.; prefers to locate in Midwest. PW-173

PHARMACIST—Graduate Philadelphia College of Pharmacy and Science 1959; 22 months' hospital pharmacy experience; registered in Pa.; desires position in the East. PW-172

STAFF PHARMACIST—Female. 1957 graduate of the University of Buffalo College of Pharmacy. Registered in New York State. Prefers to locate in the East. PW-171

CHIEF PHARMACIST OF ASST. CHIEF PHARMACIST—Graduate University of Pittsburgh College of Pharmacy, 1956. Registered in Ohio and Pa. Staff pharmacist experience in making sterile solutions, bulk compounding, student nurse instruction, formulary development and purchasing. One year's experience as chief pharmacist with supervisory responsibilities. Available within 30 days and will locate in any section of the United States. PW-169

PHARMACIST—Registered in Iowa and S.D. Prefers to locate in Mich., Colo. or Ariz. Management experience. PW-167

PHARMACIST—Female. Graduate of the University of Idaho, 1954. Registered in Ill. Hospital Experience. Prefers Chicago area. PW-166

PHARMACIST—Graduate of Long Island University and the University of Louisville. Prefers position in Ky. or Va. area. PW-165

CHIEF OR ASST. CHIEF PHARMACIST—Female. B.S. and M.S. Purdue University. Ten years' hospital pharmacy experience. Registered in Ind. and Ky. PW-164

STAFF PHARMACIST—Young female pharmacist from Taiwan would appreciate position in U.S. teaching hospital with opportunity to learn more about hospital pharmacy. Has experience as manufacturing pharmacist at National Taiwan University Hospital. PW-163

STAFF OR ASST. CHIEF PHARMACIST—Male. Served hospital pharmacy internship. One year's additional experience. Registered in Minn. and Wash. Prefers to locate in West. PW-162

PHARMACIST—Male. Registered in La. and Mo. Experienced. Prefers Midwest. PW-161

STAFF PHARMACIST—Female. Prefers location in long term illness-type institution. Registered in Calif. and Ohio. Experienced. PW-160

STAFF PHARMACIST—Male, married. Registered N. Y. and N. J. Prefers New England. PW-157

CHIEF PHARMACIST—Female, single. B.S. Registered R. I. Eight years' hospital pharmacy experience. PW-156

ASST. CHIEF PHARMACIST—Male, single. Registered N. Y. and Vt. Served hospital pharmacy internship; now employed part-time staff pharmacist. Prefers Eastern part of country. Has M.S.; 4 years' hospital pharmacy experience. PW-154

ASST. PHARMACIST—Male, married. B.S. Served hospital pharmacy internship. Experienced hospital pharmacist, research pharmacist and retail pharmacist. PW-151

CHIEF PHARMACIST—Male, married. B.S. Ten years' hospital pharmacy experience. Registered Mass., Ill., Mo., Ky., Tenn. and Va. PW-150

PHARMACIST—Male, single. B.S. pharmacy, June 1959. Locate East. PW-149

ASST. CHIEF OR CHIEF PHARMACIST—Single, male. Registered in D. C., Ill., Md., and Pa. Graduate University of Pittsburgh in 1953; experience in research. Prefers North and East. PW-148

CHIEF PHARMACIST—Registered in Mo. and Ill. Ph.G. degree. Eight years' experience in hospital pharmacy. PW-147

STAFF PHARMACIST—Male, single. Completed military requirements. Hospital pharmacy experience. Prefers East. PW-146

CHIEF PHARMACIST—Registered in N. J. Any location. Six years' experience in hospital pharmacy. PW-145

CHIEF PHARMACIST—Prefers N. Y. or N. J. area. Over 20 years' experience as chief pharmacist and purchasing agent. Graduate St. John's University College of Pharmacy and registered in N. Y. and N. J. PW-144

STAFF PHARMACIST—Female, single. Registered Philippines. M.S. pharmacy, St. Louis College of Pharmacy. Locate any section of country. PW-143

ASST. CHIEF PHARMACIST—Male, married. B.S. pharmacy. Registered N. Y. Hospital and retail experience. Locate N. Y. State. PW-142

CHIEF PHARMACIST—Male, married. B.S. Conn. registration. Five years' hospital pharmacy experience. Prefers Northeast section of country. PW-140

STAFF PHARMACIST—Female, married. Registered Kansas. Four years' hospital pharmacy experience. PW-136

PHARMACIST—Male, single. Registered Conn. and N. J. Five years' hospital pharmacy experience. B.S. Prefers Conn. or Texas. PW-123

ASST. DIRECTOR OR DIRECTOR OF PHARMACY SERVICES—Male, single. B.S. Retail and five years' hospital experience. Registered Ill. PW-119

STAFF PHARMACIST—Female, single. Registered Mo. B.S. Hospital pharmacy experience. Desires to locate in Midwest. PW-104

positions open

ASST. CHIEF PHARMACIST—Woman preferred. Must have Pa. registration. Duties include filling prescriptions and small volume of manufacturing. Forty-hour week, 7 holidays per year, 7 sick days per year. PO-139

CHIEF PHARMACIST—65 bed (increasing to 100 bed) general hospital located in N. Y. Carry out functions of pharmacy dept. Opportunity to be named Chief Purchasing Agent and be chief purchaser for the hospital. Forty-hour week, up to 3 weeks' vacation, located in low cost living area. PO-138

CHIEF PHARMACIST—495 bed general hospital located in Va. Responsible to superintendent for management of pharmacy personnel, solution manufacturing, purchase of all pharmaceutical items and supervision of compounding and dispensing drugs. Lecture student nurses. Must be registered, hospital experience preferred. Varied working hours; 3 weeks' vacation. Benefits include meals while on duty, hospitalization insurance, if single —room available. PO-137

CHIEF PHARMACIST—250 bed general hospital located in Rochester, N. Y. Must be registered in N. Y. Hospital experience helpful, but not essential. Forty-hour week. Liberal personnel policies. PO-136

CHIEF PHARMACIST—70 bed general hospital, located in N. C. Responsible for establishing a pharmacy department and assisting in the purchasing department. Generous benefits. PO-135

CHIEF PHARMACIST—150 bed general hospital, located in N. M. To assume complete charge of purchasing and distribution drugs. PO-134

CHIEF PHARMACIST—96 bed general hospital, located in Montana. Responsible for the procurement, dispensing, control and in-service education program concerning drugs. Generous benefits. PO-133

STAFF PHARMACIST—75 bed general, private hospital located in Indiana. State registration required. Male or female. PO-131

STAFF PHARMACIST—300 bed general hospital. Inpatient orders - no bulk compounding. Must be eligible for Ill. registration. Forty-four hour week, 2 weeks' vacation. PO-130

CHIEF PHARMACIST—120 bed general, non-profit hospital. Individual will have complete charge of ordering, dispensing and charging of medical supplies. Male or female. Registration in Ohio required. Forty - forty-eight hour week, 2 weeks vacation, other generous hospital benefits. PO-129

ASST. CHIEF PHARMACIST—325 bed hospital; 40-hour week; 4 weeks' vacation. Must be eligible for registration in Pa. PO-128

CHIEF PHARMACIST—185 bed private non-profit hospital located in Va. Prefer applicant with hospital pharmacy internship and 1 year's experience. PO-126

STAFF PHARMACIST—450 bed general hospital located in Ohio. PO-124

ASST. CHIEF PHARMACIST—3,300 bed psychiatric hospital. To assist in the reorganization of the department. Eligible for registration in Ohio. Two years' experience preferred. PO-123

CHIEF PHARMACIST—60 bed mission hospital operated by Presbyterian National Missions; extensive outpatient department; on Navajo Indian Reservation near Gallup, N. M. Qualified to register in Ariz.; single man or woman, challenged by service rather than benefits. PO-122

SENIOR PHARMACIST—325 - expanding to 500 - bed university hospital. Requirements: B.S., registration in Calif., hospital pharmacy internship, supervisory experience. Forty-hour week, 3 weeks' vacation. PO-119

STAFF PHARMACIST—250 bed hospital. Ohio registration, experience not necessary. Forty-hour week, 2 weeks' vacation. Scheduled salary increases. PO-118

STAFF PHARMACIST—1,000 bed general hospital. Eligible for registration in Ohio. Large O.P.D. Clinic. B.S. required. Forty-hour week, 2 weeks vacation. PO-117

STAFF PHARMACIST—150 bed general hospital. Only female considered. Must be elibible for Ill. registration. Hospital experience desirable, but not necessary. Forty-hour week, 2 weeks' vacation. PO-116

ASST. CHIEF PHARMACIST—425 bed general hospital; duties include dispensing and supervision of special projects. Prefer male applicant with internship in hospital pharmacy. Unique opportunity to obtain experience. PO-115

CHIEF PHARMACIST—150 bed general hospital. To assume complete responsibility for the pharmacy department. Three weeks' vacation; discount on meals and hospitalization. PO-114

CHIEF PHARMACIST—340 bed general hospital in South; affiliated with medical school; outpatient clinic and hospital pharmacy internship program. PO-112

STAFF PHARMACISTS—Two—Eligible for licensure in West Va. and Ky. PO-111

STAFF PHARMACIST—320 bed general hospital. Must be eligible for State of Wash. license. Experience in hospital pharmacy desirable. Forty-hour week, 2 weeks' vacation and other benefits. PO-110

CHIEF PHARMACIST—244 bed hospital. Calif. registration required. Complete charge of pharmacy including all purchasing. Forty-hour week, 2 weeks' vacation. PO-106

STAFF PHARMACIST—215 bed general hospital expanding to 35 more beds. N. Y. registration required as well as hospital experience. Forty-hour week, 2 weeks' vacation. PO-104

CHIEF PHARMACIST—73 bed general hospital. Complete responsibility of Pharmacy Dept. Forty-four hour week, 2 weeks' vacation. PO-102

ASST. CHIEF PHARMACIST—152 bed general hospital expanding to 180 beds. Registration in Neb. required. Forty-hour week, 2 weeks' vacation. PO-101

STAFF PHARMACIST—400 bed general hospital located in Iowa. Forty-hour week, 2 weeks' vacation. PO-99

CHIEF PHARMACIST—425 bed hospital. Male preferred. Mo. registration required. Will train good applicant. Forty-hour week. PO-98

STAFF PHARMACIST—400 bed general hospital. Eligible registration in Fla. Forty-hour week. PO-96

STAFF PHARMACIST—500 bed general hospital located in Okla. B.S. required. Forty-hour week. PO-95

ASST. CHIEF PHARMACIST—315 bed general hospital. Registration in Iowa required. Experience desirable. Forty-hour week, 2 weeks' vacation. PO-92

STAFF PHARMACIST—400 bed general hospital. Internship in hospital pharmacy preferred. Eligible for Tex. registration. Forty-hour week; 2 weeks' vacation. PO-90

STAFF PHARMACIST—316 bed general hospital. Eligible registration in Minn. Some manufacturing. Forty-hour week; 2 weeks' vacation and other benefits. PO-81

ASST. CHIEF PHARMACIST—237 bed general hospital in West Va. Female desired. Forty-four hour week, 2 weeks' vacation. PO-77

STAFF PHARMACIST—335 bed hospital located in Fla. Duties include responsibilities in outpatient department and parenteral solution room. Forty-hour week, 2 weeks' vacation and 1 meal daily. PO-75

CHIEF PHARMACIST—265 bed general hospital. Varied duties including teaching if interested. Forty-hour week, 2 weeks' vacation. PO-74

CHIEF PHARMACIST—325 bed general hospital. Eligible for registration N. Y. Hospital experience desirable. Forty-hour week, 2 weeks' vacation. PO-70

STAFF PHARMACIST—325 bed research hospital. Minimum 2 years' experience, preferably in hospital pharmacy. N. Y. registration required. Duties include manufacturing sterile solutions and assisting in product development. Research work beyond 40-hour week available at hourly rate. PO-61

CHIEF PHARMACIST—88 bed hospital located in Pa. Planning expansion to 125 beds for general patients and 40 beds for chronic patients. Possibility for pharmacist to serve as Asst. Adm. in charge of Purchasing, Central Supply, and Store Room. Forty-hour week, 2-4 weeks' vacation. Young man preferred. PO-59

ASST. CHIEF PHARMACIST—Large voluntary hospital located in Brooklyn; N. Y. registration required. Supervisory ability needed. Thirty-five hour week, 2 weeks' vacation; 10 days' sick leave; 9 holidays. PO-51

STAFF PHARMACIST—460 bed general hospital in Mass. Forty-hour week, 2 weeks' vacation, other benefits. PO-40

ASST. CHIEF PHARMACIST—310 bed general hospital located in Va. Forty-hour week, 2 weeks' vacation, 3 weeks' sick leave, 6 holidays. Also STAFF PHARMACIST in same hospital. Experience preferred; 40-hour week, 2 weeks' vacation. PO-35

STAFF PHARMACIST—550 bed general hospital located in Ohio. Forty-hour week; 2 weeks' vacation. PO-34

CHIEF PHARMACIST—350 bed hospital. Must be eligible for licensure in N. J.; interest in manufacturing; 44-hour week, 2 weeks' vacation. PO-6

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August, 1959